



HyPerforma 5.1 Single-Use Bioreactor (S.U.B.) User's Guide

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Warn-, Sicherheits- und Gewährleistungsinformationen

Herzlichen Glückwunsch! Sie haben ein qualitativ hochwertiges Gerät von Thermo Scientific erworben. Wir haben in dieses Benutzerhandbuch Sicherheitsinformationen aufgenommen, die auf unserem Wissen und unserer Erfahrung basieren. Es ist jedoch wichtig, dass Sie mit Ihrer Sicherheitsmanagement-Abteilung zusammenarbeiten, um sicherzustellen, dass dieses Gerät in Ihre Sicherheitspraxis integriert wird. Bitte nehmen Sie sich etwas Zeit, um Ihre eigene Arbeitssicherheitsanalyse zur Ermittlung und Prüfung aller potenziellen Risiken durchzuführen.



WARNUNG: Lesen Sie dieses Benutzerhandbuch aufmerksam durch, bevor Sie das Gerät in Betrieb nehmen.

Der HyPerforma™-Einweg-Bioreaktor (Single-Use Bioreactor, S.U.B.) von Thermo Scientific™ ist für den Betrieb unter herkömmlichen Bedingungen eukaryotischer Zellkulturen ausgelegt. Allgemeine Kenntnisse in Bezug auf Bioreaktorsysteme und deren Betrieb sind wichtige Voraussetzungen für die erstmalige Verwendung dieses Systems. Lesen Sie dieses Benutzerhandbuch vor der Inbetriebnahme aufmerksam durch; andernfalls kann es zu Verletzungen und zum Verlust des Produkts kommen.



WARNUNG: Gefährliche Spannungen im Innern.

Der Mischer-Motor, die Motorsteuerung und Steuerkonsole bestehen aus elektrischen Komponenten. Es besteht Verletzungs- und Stromschlaggefahr. Vor dem Öffnen elektrischer Komponenten ist die Stromversorgung zu unterbrechen. Wartungsarbeiten dürfen nur von zertifiziertem Personal durchgeführt werden.

Thermo Fisher Scientific empfiehlt den Einsatz von Standard-Verriegelungsmaßnahmen bei Arbeiten an elektrischen Bauteilen. Der Hauptschalter an der elektrischen Steuerkonsole (E-Box) kann gesperrt werden.



WARNUNG: Es kann zu elektrostatischer Aufladung in den BPC kommen.

- Die BioProcess-Container (BPC) können als Isolatoren für elektrostatische Aufladung fungieren. Wenn elektrostatische Aufladung an einen BPC übertragen wird, kann sich die Ladung im BPC bzw. im Produkt innerhalb des BPC akkumulieren. Dieses Phänomen variiert je nach Produkt und Anwendung; daher liegt es in der alleinigen Verantwortung des Endnutzers sicherzustellen, dass eine Gefährdungsbeurteilung durchgeführt und das Risiko eines elektrostatischen Schocks ausgeschlossen wird.
- Sofern möglich, kann ein Produkt-Adapter aus Edelstahl am Rahmen geerdet werden, um die elektrostatische Aufladung aus dem Material innerhalb des BPC abzuführen. Es empfiehlt sich, die elektrostatische Aufladung durch Erdung aller BPC abzuführen, bevor es zu einer Berührung kommt. Beim Arbeiten mit BPC wird der Einsatz von nichtleitendem Material empfohlen, dazu zählt beispielsweise die Verwendung nichtleitender Handschuhe.



WARNUNG: Rotierende Bauteile – Gefahren durch Hängenbleiben oder Einklemmen.

Rotierende und bewegliche Teile, wie z. B. die Motorhalterung für 1.000-Liter- und 2.000-Liter-Systeme, können Verletzungen verursachen. Halten Sie Ihre Hände während des Betriebs von beweglichen Teilen fern.

- Betreiben Sie dieses Gerät nicht ohne die mitgelieferte und ordnungsgemäß montierte und funktionierende Schutzvorrichtung.
- Es liegt in der Verantwortung des Endbenutzers, sicherzustellen, dass diese Vorrichtung ordnungsgemäß funktioniert, dass alle Schutzvorrichtungen in gutem Betriebszustand sind und dass das gesamte Bedienpersonal ausreichend ausgebildet und sich der Gefahren durch Hängenbleiben oder Einklemmen und den damit verbundenen Schutzvorkehrungen, wie Warnschilder und Schutzvorrichtungen, bewusst ist.



WARNUNG: Verwenden Sie Leitern und erhöhte Plattformen mit Vorsicht.

Einige Vorgänge, z. B. das Laden eines BPC in einen großen S.U.B., erfordern den Einsatz einer Leiter oder einer Plattform. Stellen Sie vor der Benutzung sicher, dass die Leiter geprüft und für das Gewicht des Benutzers ausgelegt ist. Wenn Sie eine Leiter oder Plattform verwenden, stellen Sie sicher, dass diese stabil ist, dass drei Kontaktpunkte (Hände und Füße) beibehalten werden und dass die Stufen sauber sind.

WARNUNG: Befolgen Sie Lockout-/Tagout-Verfahren.

Zur Vermeidung von Verletzungen bei der Wartung der Ausrüstung müssen die in Ihrem Unternehmen gültigen Lockout-/Tagout-Verfahren angewendet werden, sodass elektrische, mechanische, pneumatische, hydraulische, chemische, thermische, Gravitationsenergie oder andere Energie isoliert werden kann und die Arbeiter vor der Freisetzung gefährlicher Energie geschützt sind.

WARNUNG: Lassen Sie bei der Handhabung von gefährlichen Chemikalien oder Materialien stets Vorsicht walten.

Das Wartungspersonal muss mit den Gefahren von Chemikalien oder Materialien vertraut sein, die sich auf oder in der Ausrüstung befinden. Verwenden Sie allgemeine Kommunikationsmethoden zum Hinweisen auf Gefahren, wie etwa Sicherheitsdatenblätter, Beschriftungen und Piktogramme, um auf Gefahren hinzuweisen.

WARNUNG: Möglicherweise beengte Räume.

Die Bediener können in größere S.U.B.-Systeme einsteigen. Bewerten Sie dieses Gerät anhand Ihrer Normen und Verfahren für beengte Räume.



WARNUNG: Gefahr des Berstens—unter Druck stehende Luft.

Der Einwegbioreaktor (S.U.B.) Die BPC-Kammer steht unter normalen Betriebsbedingungen unter leichtem Druck. Die normale passive Entlüftung verhindert überschüssigen Druckaufbau innerhalb der Kammer. Der Druck in der Kammer und in der Zufuhrleitung sollte auf die korrekte Einstellung hin überwacht werden.

- Behälterinhalt steht unter Druck
- Der BPC-Druck darf 0,03 bar (0,5 psi) nicht überschreiten.
- Der Einlassdruck darf 0,34 bar (5 psi) nicht überschreiten.
- Stellen Sie sicher, dass der EntlüftungsfILTER richtig positioniert ist und richtig funktioniert.



WARNUNG: Heiße Oberflächen. Nicht berühren.

Der Heizmantel ist dazu konstruiert, um die innere Behälterwand zu erwärmen. Unter normalen Betriebsbedingungen erzeugt der Motor Wärme und möglicherweise heiße Oberflächen.

- Heiße Oberfläche innen
- Bei Berührung kann es zu Verbrennungen kommen
- Während des Betriebes nicht berühren



WARNUNG: Quetschgefahr.

Der Motorlift auf 1.000-Liter- und 2.000-Liter-S.U.B.-Systemen kann mit der Handsteuerung gehoben und gesenkt werden. Bei der Positionsänderung des Motors ist Vorsicht geboten, um das Einklemmen eines Bedieners oder die Beschädigung des Geräts oder BPC zu vermeiden.



WARNUNG: Der Thermo Scientific HyPerforma Einweg-Bioreaktor darf gemäß der geltenden EU-ATEX-Richtlinie nicht in explosionsgefährdeten Bereichen installiert werden.

Es liegt in der Verantwortung des Endnutzers, die in der ATEX 2014/34/EU-Richtlinie aufgeführten potenziellen Gefahren zu prüfen und zu berücksichtigen.

Schutzerdung

Die Schutzerdung muss überprüft werden, bevor der S.U.B. an eine Steckdose angeschlossen wird. Stellen Sie sicher, dass die Steckdose korrekt geerdet ist.

Umgebungsbedingungen

- Betrieb: 17 bis 27 °C; 20 bis 80 % relative Luftfeuchtigkeit, nicht kondensierend
- Lagerung: -25 bis 65 °C
- Installationskategorie II (Überspannung) gemäß IEC 664
- Höhenlimit: 2.000 Meter

Elektrische Anschlüsse

Die Stromversorgung sollte durch einen 15-A-Stromkreis (nicht-GFCI) erfolgen. Erdungsfehler treten auf, wenn der Strom an einer Stelle entweicht und Elektrizität in Richtung Erde austritt. **Ein Stromschlag kann auftreten, wenn der Stromweg zur Erde über den menschlichen Körper verläuft.** Ein FI-Schutzschalter (GFCI) erkennt den Stromverlauf zur Erde und unterbricht die Stromversorgung (Auslösen des FI-Schutzschalters) innerhalb eines Bruchteils einer Sekunde, wobei die Stromstärke deutlich unterhalb des gefährlichen Wertes bleibt. Aufgrund der Empfindlichkeit des FI-Schutzschalters gegenüber Kriechstrom (bereits bei geringem mA-Wert) empfiehlt es sich, dass der Einweg-Mischer NICHT an eine Steckdose mit Fehlerstromschutz angeschlossen wird.

Informationen zum Wassermantelbehälter

S.U.B.-Hardware-Einheiten mit Wasserummantelung sind für den Betrieb mit Wasser als Wärmeträger mit Temperaturen von maximal 50 °C (122 °F) bei einem Betriebsdruck von weniger als 1 MPa (150 psig) ausgelegt. Für größtmögliche Sicherheit empfiehlt es sich, dass der S.U.B. mit maximal 75 psig betrieben wird.

Hinweis: Der Einwegbioreaktor (S.U.B.) Die BPC-Betriebsgrenzen in Bezug auf die Temperatur liegen bei 5 bis 40 °C. Der Innendruck sollte 0,03 bar (0,5 psi) nicht überschreiten. Der Wassermantel muss nicht gemäß Abschnitt U-1(c)2(f) der ASME-Richtlinien für Boiler und Druckbehälter registriert, kontrolliert und mit dem Code-„U“-Stempel versehen sein bzw. unterliegt nicht der Druckgeräterichtlinie 97/23/EG des Europäischen Parlaments („Pressure Equipment Directive“, PED). Auf Anfrage kann eine Konformitätserklärung in Bezug auf die für PED geltende gute Ingenieurpraxis zur Verfügung gestellt werden.

Einsatz von Rührdrehzahlreglern und Sicherheitsverriegelungen

Die in der Bioreaktorsteuerung integrierten Rührdrehzahlregler dienen zur Begrenzung der maximalen Mischgeschwindigkeit entsprechend der vordefinierten Flüssigkeitsmengen. Sicherheitsabschaltungen, die das Rühren stoppen, wenn das Volumen in einem S.U.B. unter definierte Grenzen fällt, und drehzahlbasierte Regler verhindern eine Beschädigung der Antriebswelle im Bioreaktor. Rührdrehzahlregler und Sicherheitsabschaltungen verhindern in der Regel die nachfolgend aufgeführten gefährlichen Situationen.



- Betrieb des Motors mit beliebiger Drehzahl unter Belastung der Antriebswelle
- Betrieb des Rührwerks bei einem Volumen von weniger als 20 % des Arbeitsvolumens des Systems
- Betrieb des Rührwerks oberhalb der empfohlenen Drehzahlbereiche, basierend auf qualifizierten Schwellenwerten für das Verhältnis von Leistungseintrag zu Volumen (P/V)

Die oben genannten gefährlichen Betriebsbedingungen müssen vermieden werden, um eine hohe Zuverlässigkeit zu gewährleisten. Die Verwendung von Sicherheitsabschaltungen und Rührgeschwindigkeitsreglern eliminiert die Möglichkeit menschlicher Fehler, welche die Zuverlässigkeit des Systems beeinträchtigen könnten. Sowohl die Flüssigkeitsmenge im Behälter als auch die auf das Laufrad einwirkende Kraft beeinflussen die Auslenkung der Antriebswelle. Eine zu große Auslenkung und/oder zu hohe Mischerdrehzahl kann die Antriebswelle beschädigen.

Weitere Informationen über den Einsatz von P/V- und Sicherheitsabschaltungen in 2.000-L-Bioreaktorsystemen finden Sie im Abschnitt 3.6.5 dieser Publikation.

Gewährleistungsinformationen

Von jeglichen Gewährleistungen (sofern anwendbar) für dieses Gerät werden folgende Fälle ausgenommen: (a) normaler Verschleiß; (b) Unfall, Katastrophe oder Ereignis höherer Gewalt; (c) unsachgemäße Verwendung, Fehler oder Fahrlässigkeit des Kunden; (d) Verwendung des Produkts in einer anderen als der vorgesehenen Art und Weise; (e) produktfremde Ursachen wie z. B. Stromausfall oder Spannungsstöße; (f) unsachgemäße Lagerung und Handhabung des Geräts; (g) Verwendung des Produkts mit Geräten oder Software von Fremdanbietern; (h) Geräte, die Ihnen als „gebrauchte“ Produkte verkauft wurden; (i) Kontakt mit unsachgemäß verwendeten oder nicht zugelassenen Chemikalien oder Proben; (j) Installation, Entfernung, Verwendung, Wartung, Lagerung oder Handhabung in unsachgemäßer, unangemessener oder nicht zugelassener Weise, wie z. B. (aber nicht ausschließlich) Nichtbeachtung der Dokumentation oder Anweisungen in den gelieferten Produkten oder in Bezug auf die Ausrüstung oder den Betrieb außerhalb der angegebenen Umwelt- oder sonstigen betrieblichen Spezifikationen oder der Betrieb mit nicht zugelassener Software, nicht zugelassenen Materialien oder anderen nicht zugelassenen Produkten; (k) Herstellung gemäß den von Ihnen angegebenen Anforderungen; (l) Installation von Software oder die Kopplung oder Verwendung des Geräts in Kombination mit Software oder Produkten, die von uns nicht genehmigt wurden; (m) Verwendung der gelieferten Produkte oder jeglicher Dokumentation zur Unterstützung von behördlichen Genehmigungen; (n) Leistung, Wirksamkeit oder Kompatibilität von spezifizierten Komponenten und (o) Leistung von kundenspezifischen Geräten oder Produkten oder spezifizierten

Komponenten oder das Erreichen von Ergebnissen des Geräts, der spezifizierten Komponenten oder Dienstleistungen innerhalb der von Ihnen gewünschten Bereiche, selbst wenn diese Bereiche uns mitgeteilt werden und in Spezifikationen, einem Angebot oder einer Arbeitserklärung beschrieben sind. **DARÜBER HINAUS FÜHREN JEDE INSTALLATION, WARTUNG, REPARATUR, INSTANDHALTUNGSMASSNAHME, VERLEGUNG ODER ÄNDERUNG AN (BZW. VON) DEM GERÄT ODER ANDERE MODIFIKATIONEN AN DEM GERÄT, DIE VON EINER ANDEREN NATÜRLICHEN ODER JURISTISCHEN PERSON ALS UNSEREM UNTERNEHMEN OHNE UNSERE VORHERIGE SCHRIFTLICHE GENEHMIGUNG DURCHGEFÜHRT WERDEN, ODER JEDE VERWENDUNG VON ERSATZTEILEN, DIE WIR NICHT GELIEFERT HABEN, ZUM SOFORTIGEN ERLÖSCHEN UND ZUR AUFHEBUNG ALLER GEWÄHRLEISTUNGEN IN BEZUG AUF DAS BETROFFENE GERÄT. WENN DAS GERÄT IN DEN VEREINIGTEN STAATEN VERWENDET WERDEN SOLL, KANN DIE GARANTIE ERLÖSCHEN, WENN SIE DAS GERÄT IN GEBIETE AUSSERHALB DER VEREINIGTEN STAATEN VERSENDEN.**

Nutzungsbeschränkungen

Dieses Gerät darf nur in Übereinstimmung mit unserer Dokumentation und (sofern zutreffend) mit anderen durch uns erteilten Anweisungen verwendet werden. Diese Anweisungen umfassen unter anderem auch eine Produktkennzeichnung mit „Nur für Forschungszwecke“ oder mit „beschränkte Nutzung“ für eine beschränkte Lizenz. Dieses Gerät ist für den Forschungsgebrauch oder die Weiterverarbeitung in Bioprocessing-Anwendungen bestimmt und nicht für den diagnostischen Gebrauch oder die direkte Verabreichung an Menschen oder Tiere vorgesehen. Wir reichen das Gerät nicht zur behördlichen Überprüfung durch eine Regierungsbehörde oder andere Organisation ein, und wir validieren das Gerät nicht für den klinischen oder diagnostischen Gebrauch, in Bezug auf die Sicherheit und Wirksamkeit oder für eine andere spezifische Verwendung oder Anwendung.

Seismische Leitlinien

Der Käufer des Systems ist dafür verantwortlich, dass länderspezifische Vorschriften und seismische Werte für die Eignung der Installation des Systems und die Sicherheit am vorgesehenen Standort bewertet werden. Darüber hinaus liegt es in der Verantwortung des Käufers, die Gebäudestruktur für das vorgesehene System zu beurteilen, um die korrekte Auslegung für die seismische Verankerung und Befestigung des Systems und der Anlage zu gewährleisten. Dem Käufer wird dringend empfohlen, sich mit einem lokalen, lizenzierten Architektur- und Ingenieurbüro in Verbindung zu setzen, um vor der Installation des Systems in der Einrichtung eine geeignete technische Analyse und abgestempelte Dokumentation bereitzustellen. Darüber hinaus ist der Käufer für die Verzerrung und Verankerung des Systems an einem dafür vorgesehenen, festen Ort verantwortlich. Thermo Fisher ist auf Anfrage gegen eine vereinbarte Gebühr gerne bei der Erstellung gesetzeskonformer seismischer Verankerungs- und Befestigungskonzepte für erworbene Systeme auf der Grundlage baulicher und länderspezifischer Vorschriften behilflich.

Es wird auch darauf hingewiesen, dass bewegliche Anlagen (d. h. Anlagen, die nicht fixiert oder auf Rollen montiert sind) gemäß ASCE 7-16, Kapitel 13, Abschnitt 1.4, von den Anforderungen an die seismische Auslegung ausgenommen sind. Obwohl diese Anlagen von den Anforderungen der ASCE 7 an die seismische Auslegung ausgenommen sind, ist zu beachten, dass solche Geräte bei einem seismischen Ereignis umsturzgefährdet sind. Daher liegt es in der Verantwortung des Käufers, sich mit der Erdbebensicherheit für bewegliche Systeme in der vorgesehenen Einrichtung zu befassen.

How to use this guide

Scope of this publication

This user's guide contains information about the standard Thermo Scientific™ HyPerforma™ 5.1 S.U.B. systems, including hardware, components, product design verification methods, installation, operation, and specifications. It is intended for use by people who may or may not have experience with Thermo Scientific systems, but who have some knowledge of bioproduction processes and large-scale mixing systems.

Revision	Date	Section	Change made	Author
A	10/2016	--	Initial release	S. Jelus/E. Hale
B	02/2017	Warnings and Safety	Added pinch hazard and potential confined space warnings to Warnings and Safety information	E. Hale
B	02/2017	Warnings and Safety	Added information about safety interlocks to Warnings and Safety information	S. Jelus
B	02/2017	2.2.4	Added number information and photo of ends of multiple-section drive shaft	S. Jelus/E. Hale
B	02/2017	3.6.4	Added warning note about agitation rate and volume requirements, and the use of safety interlocks	S. Jelus/E. Hale
B	02/2017	5.1.2	Added measurement to Table 5.1 for 2,000 L drive shafts and cross-reference to Appendix D	E. Hale
B	02/2017	3.4.3	Added information about 2-piece drive shaft, a note about the position of impeller tubing inside the BPC, and serial number information and a photo of ends of multiple-section drive shafts	S. Jelus/E. Hale
B	02/2017	1.1	Added information about and photo of the BPC bearing port cap label	E. Hale
B	02/2017	3.4.3	Added a note about not pushing drive shaft straight into the assembly when loading	S. Jelus/E. Hale
B	02/2017	3.4.3	Added information and Figure 3.102 to illustrate proper insertion of drive shaft	S. Jelus/E. Hale
B	02/2017	3.4	Added 2,000 L BPC and drive shaft loading, and condenser system setup instructions	E. Hale
B	02/2017	4.2	Added 1,000 L and 2,000 L hardware specifications	E. Hale
B	02/2017	4.2	Added information about 2-piece drive shaft to 2,000 L specifications	S. Jelus/E. Hale
B	02/2017	4.2	Added ceiling height requirements for 2-piece drive shaft and detail about mixing speed to 2,000 L specifications	E. Hale
B	02/2017	1.2.3	Added information about BPC lift for 2,000 L systems	E. Hale
B	02/2017	4.3	Added drawing of 1,000 L electrical control panel	E. Hale

Document change information

Revision	Date	Section	Change made	Author
B	02/2017	1.2.3 and 2.2.6	Added information about motor lift and handheld controller for 1,000–2,000 L systems	E. Hale
B	02/2017	2.2.5	Added information about setting the air pressure rate for motor adjustment for 1,000–2,000 L systems	E. Hale
B	02/2017	3.6.5	Added Agitation Rate Calculations section to Chapter 3	E. Hale
B	02/2017	3.3	Added 1,000 L systems to 500 L BPC loading section	E. Hale
B	02/2017	3.3.2	Added information about drive shaft serial numbers	E. Hale
B	02/2017	1.2.1	Added drawing showing 2,000 L S.U.B. features	E. Hale
B	02/2017	2.1.3	Added 1,000 L and 2,000 L electrical box preparation	E. Hale
B	02/2017	Appendix C	Added Appendix C—2,000 L S.U.B. agitator operation and maintenance guidelines	S. Jelus/ E. Hale
B	02/2017	Appendix D	Added Appendix D—Drive shaft use log	E. Hale
B	02/2017	Chapter 4	Removed 5.1 S.U.B. Made-to-order table	E. Hale
B	03/2017	3.4.3	Added image of 2,000 L 5.1 BPC hanging tag	E. Hale
B	03/2017	1.2.3	Added drive shaft specifications table	E. Hale
B	04/2017	Warnings and Safety	Added explosive atmosphere (ATEX) warning	E. Hale
B	04/2017	4.2	Changed "Maximum Mixing Rate" to "Agitation Speed Range" in hardware specifications	E. Hale
C	05/2017	Chapter 4	Corrected drive shaft diameter for 500 L S.U.B.	E. Hale
D	09/2017	3.6	Added harmonics/cavitation graph and context about these operating parameters to agitation information	E. Hale
D	09/2017	5.2, 3.4	Added a FAQ about excessive residue buildup in condenser bag due to low TCU coolant levels, and provided more information in the 2,000 L condenser system instructions	E. Hale
D	09/2017	Warnings, safety, and warranty information	Added warranty and usage information	E. Hale
D	09/2017	How to use this guide	Added a section for abbreviations/acronyms	E. Hale
D	09/2017	Chapter 4	Added noise level to specifications for all S.U.B. sizes, and corrected 2,000 L ceiling height requirement for 4-piece drive shaft loading	E. Hale
D	09/2017	Chapter 4	Added accessory part numbers, and BPC illustrations and specifications	E. Hale
D	10/2017	3.4.3	Added note that all 2,000 L drive shaft heads are now black	E. Hale
D	01/2018	--	Updated warning symbols and "Hot surface" warning	E. Hale
D	01/2018	4.2	Corrected 500 L ceiling height requirement for drive shaft loading	E. Hale
D	01/2018	3.6.5	Revised Graph 3.4 by changing 2,000 L line to 750 and 1,000 L line to 375 L	E. Hale
D	01/2018	3.6.5	Changed Table 3.4 footnote to "> 20 W/m ³ "	E. Hale
D	01/2018	3.6.5	Changed first footnote in Table 3.6 to "> 20 W/m ³ "	E. Hale

Document change information (continued)

Revision	Date	Section	Change made	Author
D	01/2018	5.1.2	Removed 2,000 L row from Table 5.1	E. Hale
D	01/2018	5.1.2	Under "Drive shaft longevity and replacement," added "of cumulative use" after "replacing your drive shaft every 360 days." In the second sentence of the second paragraph, changed to "every 180 days of cumulative use." In the first sentence of the note, added "< 50% working volume."	E. Hale
D	01/2018	3.4.3	Updated Figure 3.102 to show the new deep impeller pocket	E. Hale
D	03/2018	Chapter 4	Changed "Operating temperature range" to specifications for all S.U.B. sizes to "Ambient to 40 +/- 0.5°C (104 +/- 0.9°C)"	E. Hale
D	04/2018	--	Removed references to 2,000 L S.U.B. four-piece drive shafts	E. Hale
D	08/2018	Warnings, safety, and warranty information	Added seismic guidance	K. Leeman
E	11/2018	Warnings, safety, and warranty information	Added emphasis to "Electrical connections" section, changed "certified personnel" to "Thermo Fisher Scientific service personnel," and updated ATEX warning	E. Hale
E	11/2018	How to use this guide	Changed "Input into Thermo Scientific publications" section to "Questions about this publication"	E. Hale
E	11/2018	2.1.3, 3.6.4, 4.3	Updated text and images of the E-Box	E. Hale
E	11/2018	3.5.3	Removed references to metal probe clips	E. Hale
E	11/2018	Appendices	Removed Appendix B (AC-Tech variable speed drive settings) and renamed Appendices B through D, accordingly	E. Hale
E	11/2018	2.2.3, Various	Removed section 2.2.3 (Attaching the cable management system arm) and edited images showing the arm	E. Hale
E	12/2018	3.1.4, 3.6.4	Edited sentence (3.1.4), reworded step #2 (3.6.4)	E. Hale
E	12/2018	3.7.1	Updated accuracy in "Mixing speed verification" to +/- 1.5 rpm or 1% of setpoint, whichever is greater	E. Hale
E	12/2018	4.2	Added tolerance to "Agitation speed range" in all specifications	E. Hale
F	09/2019	4.2, Various	Minor formatting changes and updated cart length demension on Figure 4.10	T. Golightly

Document change information (continued)

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.

Publication	Description
Thermo Scientific HyPerforma 5.1 S.U.B. Validation Guide (DOC0023)	Information about validation procedures
Thermo Scientific HyPerforma 5.1 S.U.B. Data Sheets (for various sizes)	Product descriptions and ordering information
Thermo Scientific HyPerforma 5.1 S.U.B. Packing and Unpacking Guide (DOC0033)	Instructions for packing and unpacking equipment

Related publications

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

Abbreviations/acronyms

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

BPC	BioProcess Container
cGMP	Current good manufacturing practices
DO	Dissolved oxygen
ETP	Equipment Turnover Package
GFCI	Ground fault circuit interrupter
HMI	Human machine interface
ID	Inner diameter
IEC	International Electrical Code
OD	Outer diameter
PED	Pressure Equipment Directive
PID	Proportional integral derivative
P/V	Power input to volume
RTD	Resistance temperature detector
STR	Stirred tank reactor
S.U.B.	Single-Use Bioreactor
TCU	Temperature control unit
VFD	Variable frequency drive

1

HyPerforma Single-Use Bioreactor (S.U.B.) overview

Chapter contents

- 1.1 Introduction to the S.U.B.
- 1.2 Hardware characteristics
- 1.3 End user and third-party supplied components
- 1.4 BPC characteristics

1.1. Introduction to the S.U.B.

The Thermo Scientific HyPerforma Single-Use Bioreactor (S.U.B.) has been designed as a single-use alternative to conventional stirred tank bioreactors currently utilized in eukaryotic cell culture. Based on years of accepted stirred tank reactor (STR) design, the S.U.B. 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.B. an attractive alternative to its conventional STR counterpart.

The 5.1 S.U.B. allows users to take advantage of low volume mixing in addition to half and full volume, providing greater flexibility all in one system. Critical design parameters such as height-to-diameter ratios, mixer design and location, and typical control system interfaces have been maintained. A key element to 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 cell culture runs over traditional reusable systems.

The S.U.B. system consists of the following primary components:

- 1. Outer support container** with water jacket heating system
- 2. S.U.B. BioProcess Container (BPC)** that is supplied gamma irradiated
- 3. Control system for units with AC motors** for agitation
- 4. Direct drive agitation mixing assembly** with an AC or DC motor (DC motor not available for 1,000 L and 2,000 L systems), drive shaft, and impeller



Figure 1.1. 50–500 L S.U.B.s.

The **outer support container** is engineered and fabricated to fully support each BPC and allow easy access for operation. It is a stainless steel vessel that holds and supports the BPC. The outer support container contains the mixing drive and water jacketed tank on casters (2,000 L S.U.B.s are not on casters). The drive shaft is detachable and reusable, and is inserted into the BPC through the mixing assembly and into the bearing port. Load cells are standard for all 5.1 S.U.B. systems.

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

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



Figure 1.2. 2,000 L 5.1 S.U.B.

This user's guide covers the setup, operation, maintenance, and troubleshooting of all 5.1 S.U.B. systems in the following volumes: 50 L, 100 L, 250 L, 500 L, 1,000 L, and 2,000 L.

Figures 1.3–1.7 illustrate some of the standard labeling on 50 L, 100 L, 250 L, and 500 L 5.1 S.U.B. systems. Systems in these sizes include the following:

- Hanging tag labeled for "5:1 Mixing" attached to the BPC bearing port (Figures 1.3–1.4)
- Motor mount engraved with "5:1 Mixing" (Figures 1.5–1.6)
- "Usable by 5:1 drive shaft only" warning label on BPC bearing port cap (Figure 1.7)
- Drive shaft with a black head that is engraved with "5:1 Mixing."



Figure 1.3. Hanging tag on 50–500 L 5.1 BPC bearing port.

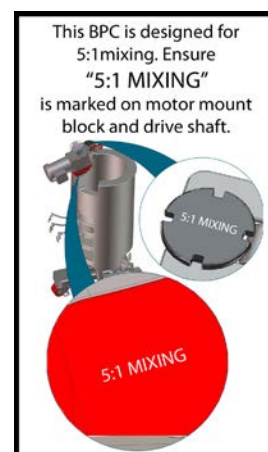


Figure 1.4. Close-up view of 5.1 BPC hanging tag.



Figure 1.5. Engraving on 50–500 L 5.1 motor mount.



Figure 1.6. Close-up view of engraving on 5.1 motor mount.



Figure 1.7. Label on 50–500 L 5.1 BPC bearing port cap.

Important notes:

- If your 50 L, 100 L, 250 L, or 500 L system components are not labeled for 5:1 mixing, consult your sales representative immediately.
- There are no 5:1 mixing labels for 1,000 L and 2,000 L S.U.B.s and BPCs.
- 5.1 S.U.B. mixing speeds should be reduced when operating at lower volumes to avoid damaging the system. For recommended agitation rates, see section 3.6.4 and the hardware specifications in section 4.2 of this user's guide.

1.2. Hardware characteristics

1.2.1. S.U.B. hardware components

Figures 1.8 and 1.9 below illustrate all available components of a 500 L S.U.B. system. **Note:** 50 L, 100 L, and 250 L systems do not have a BPC loading door, and use a one-piece drive shaft.

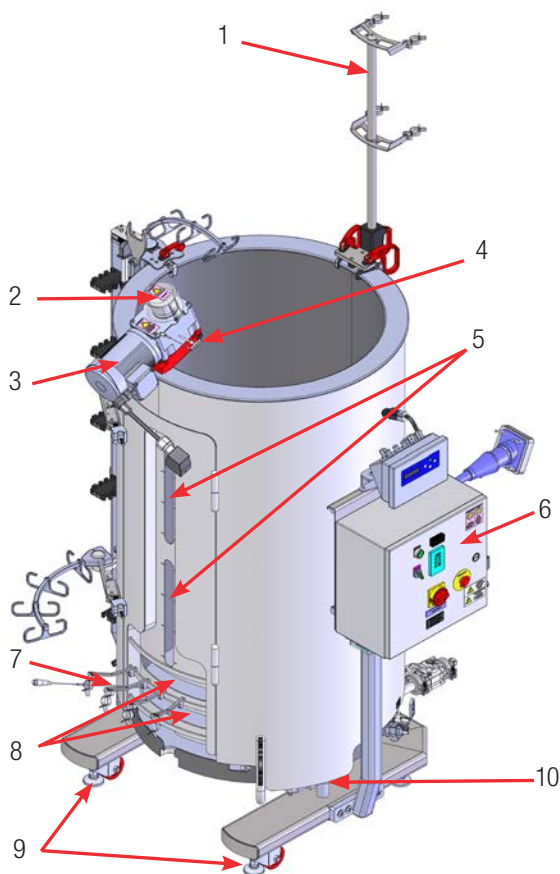


Figure 1.8. Front view of 500 L S.U.B.

1. Exhaust vent filter holder
2. Mixing assembly with shield
3. Mixer motor
4. Bearing port receiver with clamp
5. BPC loading door (500 L only) and liquid sight windows
6. Electrical control panel (E-Box), optional
7. Probe hanger bracket
8. Probe access windows
9. Leveling casters
10. Load cells

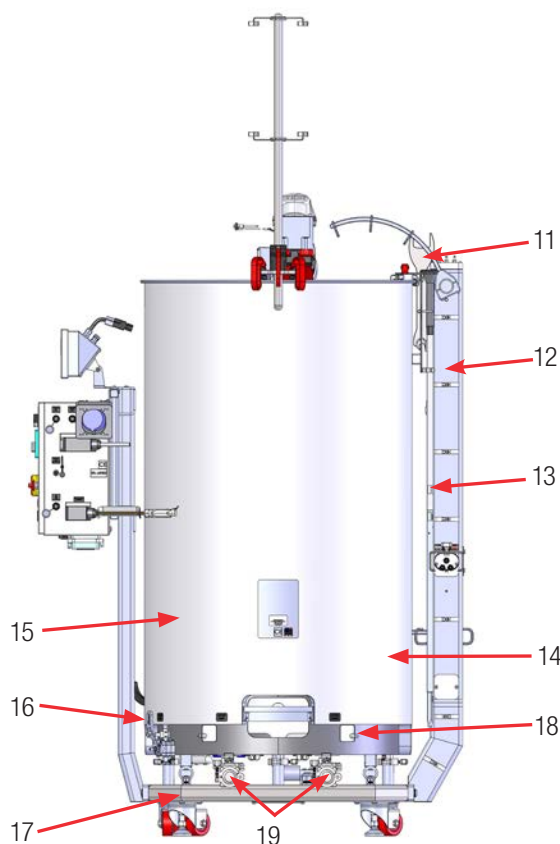


Figure 1.9. Back view of 500 L S.U.B.

11. 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
12. Cable management system
13. Drive shaft, stored (2-piece)
14. 304 Stainless steel outer support container
15. 0.95 cm (3/8 in.) Dimpled jacket
16. Bleed valve
17. Cart assembly
18. Bottom cutouts/pins for BPC attachment/alignment
19. Quick-connect water inlet/outlet ports

Figures 1.10 and 1.11 below illustrate all available components of a 2,000 L S.U.B. system. **Note:** 1,000 L systems have a cutout instead of a back access door, and do not include a BPC lift. See section 4.1.3 for a complete illustration of a 1,000 L S.U.B.

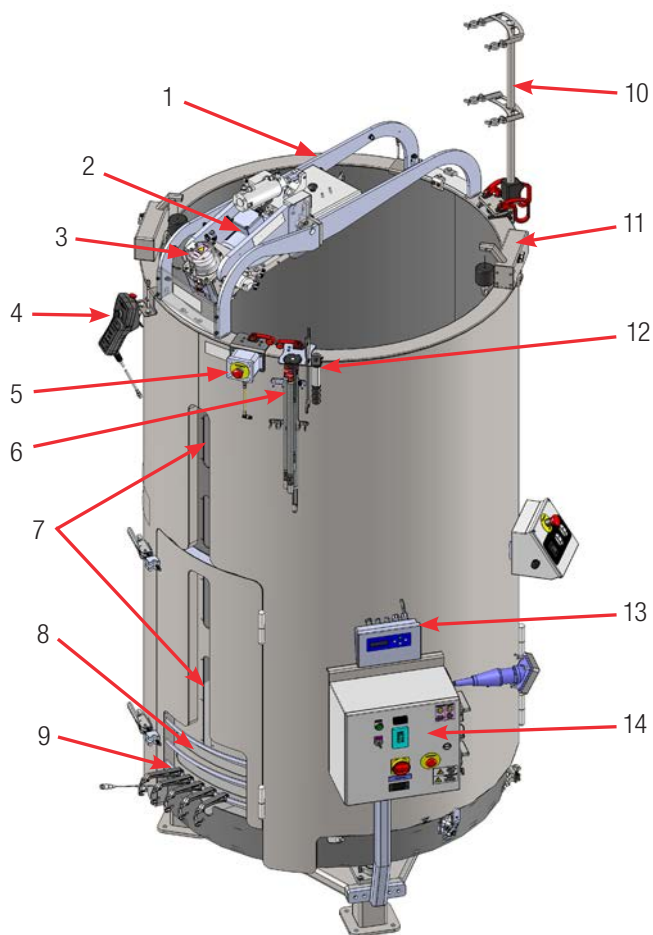


Figure 1.10. Front/side view of 2,000 L S.U.B.

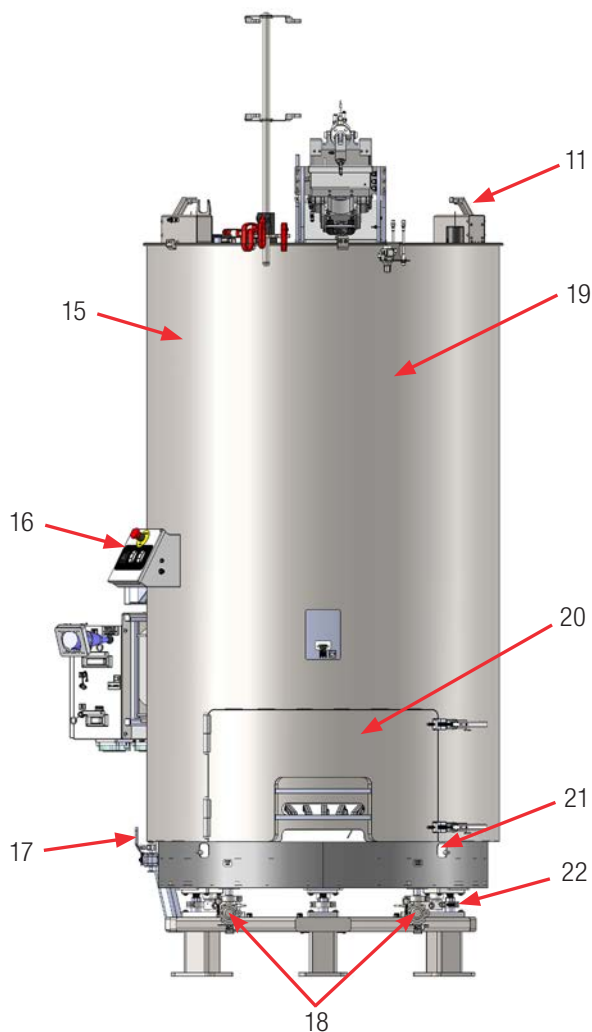


Figure 1.11. Back view of 2,000 L S.U.B.

1. Motor lift
2. Mixer motor
3. Mixing assembly with motor safety shield
4. Handheld controller for motor adjustment (on bracket)
5. Emergency stop (E-Stop)
6. Drive shaft, stored
7. BPC loading door and liquid sight windows
8. Probe access window
9. Probe hanger bracket (with probe clips)
10. Exhaust vent filter holder
11. BPC lift, for 2,000 L 5.1 S.U.B.s only (2)

12. 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
13. Load cell display
14. Electrical control panel (E-Box), optional
15. 0.95 cm (3/8 in.) Dimpled jacket
16. BPC lift control
17. Bleed valve
18. Quick-connect water inlet/outlet ports
19. 304 Stainless steel outer support container
20. Rear access door
21. Bottom cutouts/pins for BPC attachment and alignment
22. Load cell (3)

1.2.2. S.U.B. system features

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

Agitation

If your system uses an AC motor and a Thermo Scientific electrical control panel (E-Box), the stirring speed is adjusted by using the E-Box keypad interface. The agitation control interface utilizes a digital display to indicate stirring speed in units of revolutions per minute (rpm). Power is supplied to the motor by a two-position power switch. The up and down arrows on the agitation keypad adjust the stirring speed. If your 50 L, 100 L, 250 L, or 500 L system has a DC motor and is integrated and managed by a third-party controller, agitation is managed by the controller. Thermo Fisher Scientific does not provide electrical control for units with DC motors.

Bioreactor control system

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

Temperature

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

Condenser system

The condenser system is recommended for 2,000 L S.U.B. use, and is available as optional hardware for smaller systems. It cools exhaust gases and re-circulates condensate into the bioreactor.

Heating performance

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

1.2.3. Additional system components

Drive shafts

The drive shaft couples the mixing impeller that is inside the BPC to the motor. If you are using a 5.1 BPC, it is important to use the correct drive shaft. See Table 1.1 for drive shaft specifications for each S.U.B. size.

Table 1.1. Drive shaft specifications for 50–2,000 L systems.

System size	Overall shaft length	Number of pieces	Head description	Material
50 L	85.09 cm (33.5 in.)	1-piece	Black, engraved with "5:1 Mixing"	Stainless steel or aluminum
100 L	100.58 cm (39.6 in.)	1-piece	Black, engraved with "5:1 Mixing"	Stainless steel or aluminum
250 L	120.90 cm (47.6 in.)	1-piece	Black, engraved with "5:1 Mixing"	Stainless steel or aluminum
500 L	155.7 cm (61.3 in.)	2-piece	Black, engraved with "5:1 Mixing"	Stainless steel or aluminum
1,000 L	167.6 cm (66 in.)	3-piece or 4-piece	White	Stainless steel
2,000 L	215.6 cm (84.9 in.)	2-piece	Black, engraved with drive shaft length	Carbon fiber

Probe integration

The autoclave tray (Figure 1.12) holds the electrochemical probes and bellows in place during the autoclave sterilization process. Design elements include the following.

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

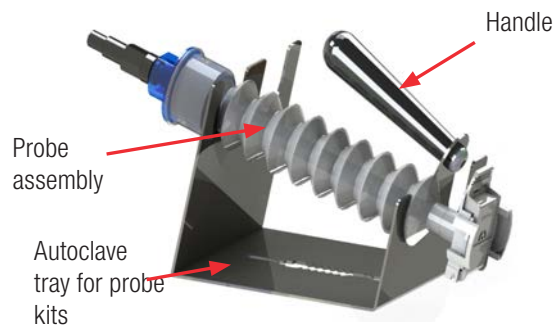


Figure 1.12. Autoclave tray and probe assembly.

The probe assembly (Figure 1.13) is an innovative design to package user-supplied pH and DO probes for sterilization, and to aseptically connect them to the BPC. The probe assembly includes an aseptic connector, molded bellows cover, and threaded probe adapter.

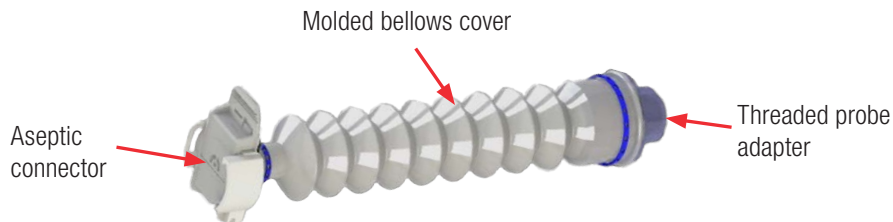


Figure 1.13. Probe assembly.

BPC lift (2,000 L systems only)

The BPC lift (Figure 1.14) helps users load the BPC into 2,000 L S.U.B.s. Two hooks, on opposite sides of the S.U.B., attach to tabs on the BPC. The BPC lift control (Figure 1.15) is used to raise and lower the BPC. For instructions on using the BPC lift, see section 3.4 of this publication.

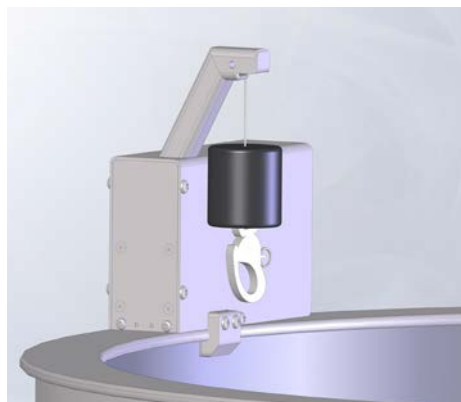


Figure 1.14. BPC lift for 2,000 L systems.

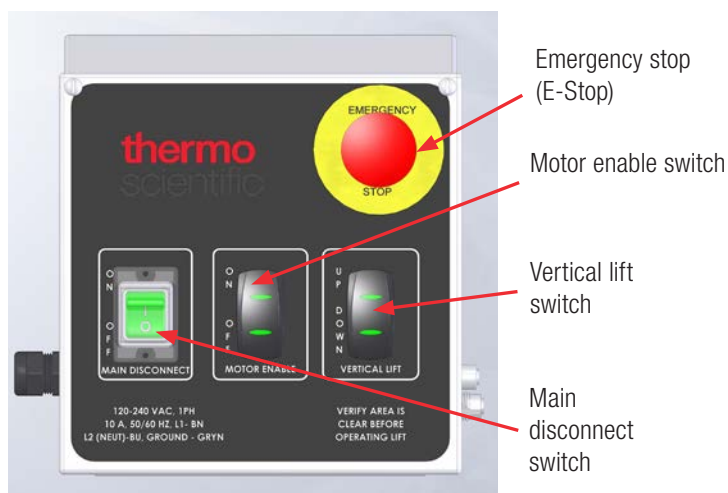


Figure 1.15. BPC lift control for 2,000 L systems.

Motor lift and handheld controller (1,000 L and 2,000 L systems only)

1,000 L and 2,000 L 5.1 S.U.B. systems include a motor lift (Figure 1.16), used to adjust the position of the motor. The motor lift is operated by a handheld controller (Figure 1.17), which is located on a bracket attached to the front of the S.U.B. For instructions on how to operate the handheld controller, see section 2.2.5 of this guide—Using the Handheld Controller for Motor Lifts (1,000 L and 2,000 L systems only).



Figure 1.16. Motor lift for 1,000–2,000 L systems.



Figure 1.17. Handheld controller for motor lifts.

Options and accessories

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

Exhaust vent filter heaters

The exhaust vent filter heater system, which includes the heater, a controller, and power cord (Figure 1.18), is available for increased longevity of the exhaust filter on the BPC. The heating element is fully insulated with molded silicone and secured around the filter by use of snap retainers, fully encapsulating the exhaust filters for consistent temperature regulation. Heating the filter sufficiently to eliminate the formation of condensation reduces the risk of fouling the filter membrane.

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



Figure 1.18. Vent filter heater.

Load cells

Load cells, which are used to determine the weight of the contents of a S.U.B., are installed on all standard 5.1 S.U.B. systems. Load cell retro-fit kits can also be added to existing S.U.B. units by a certified service technician. Load cells arrive uncalibrated. The load cell manufacturer or a qualified technician should calibrate these systems onsite.

The load cell kit comes with three load cells, summing block, wiring, and a display screen with a choice of several data interfaces (Figure 1.19).

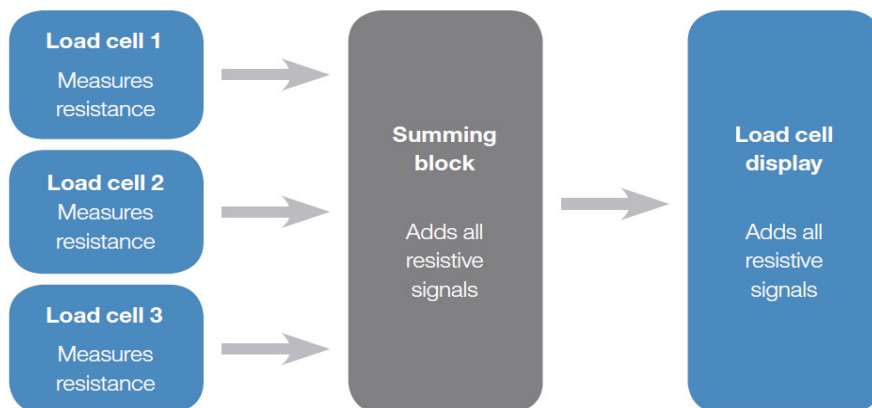


Figure 1.19. Load cell system overview.

Load cells are typically radial-mounted in sets of three. The mounting location (Figure 1.20) varies slightly for each size in order to allow easy access to the bottom drain or sparging mechanisms and tubing.



Figure 1.20. Load cell location.

AC and DC motors

AC and DC motor options are available to help tailor the S.U.B. system to your specific needs. **Note:** DC motors are only available for 50 L, 100 L, 250 L, or 500 L systems.

DC motors operate at a lower voltage and, when integrated with a controller system that receives sensor feedback, provide more accurate speed control through a digital program transmitter. The DC motor comes with an encoder, but does not come with a motor control option from Thermo Scientific. For DC motors, a control option must be specified by the end user.

AC motors may be used with the Thermo Scientific E-Box. AC motors include a variable frequency drive, and are controlled using either the provided keypad or a controller specified by the end user.

Cable management systems

The cable management system is available as an option on 50 L, 100 L, 250 L, 500 L, and 1,000 L units. It is used to organize various lines and includes the following components (Figure 1.21).

- Internal channel for sparge lines
- External channels for feed and base addition lines
- Harvest line hook

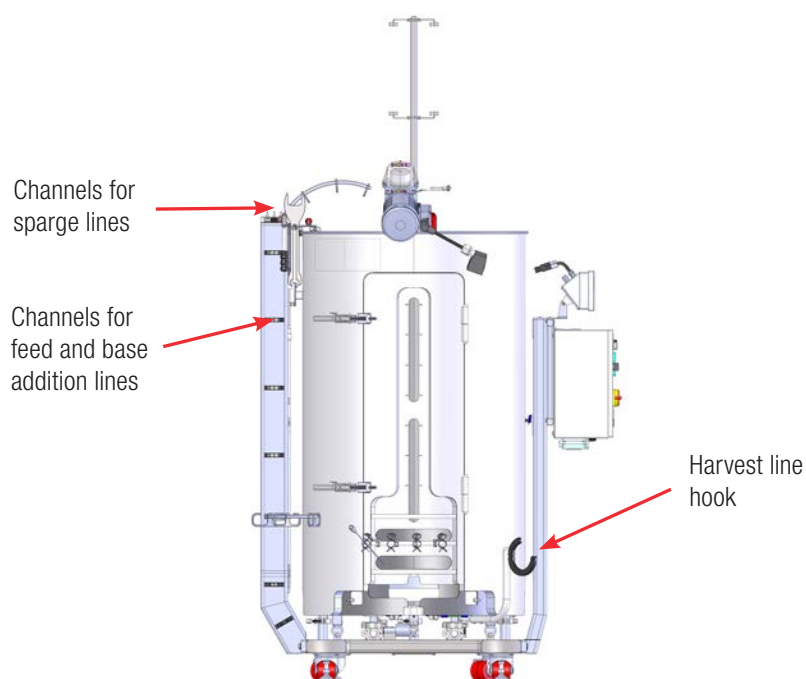


Figure 1.21. Figure 1.21. 500 L S.U.B. with cable management system.

Miscellaneous items

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

- **Sampling manifold with luer lock**
- **S.U.B. temperature sample port**—For RTD calibration/validation

- **Sparge line support**—Keeps the drilled hole sparge line in a vertical position for optimal gas flow (Figure 1.22). For more information see section 2.2—Installation and Setup.



Figure 1.22. Figure 1.22. Sparge line support.

- **Heavy-duty tubing clamps (typically four or five)**—Tubing clamps (Figure 1.23) are required for pinching off line sets that are not in use in order to prevent process fluids from moving into the line sets. Prior to sterile probe insertion, tubing clamps must be in place to close off probe ports. For more information, see the BPC and drive shaft loading instructions in sections 3.2, 3.3, and 3.4 of this publication.



Figure 1.23. Figure 1.23. Heavy-duty tubing clamps.

Note: The sparge line support is included with all standard S.U.B. units. Other items are sold separately. Please contact your sales representative for more information.

1.3. End user and third-party supplied components

1.3.1. pH and DO probes

Table 1.2 shows the length and diameter requirements for traditional sensors (probes) that can be integrated into the S.U.B. These requirements are based on the necessary insertion depth of the probe when used with the probe ports. **Note:** The presence of a properly positioned O-ring on the probe is critical for use with the S.U.B.

Table 1.2. Manufacturers and models of compatible pH/DO probes.

Probe lengths (from O-ring to tip) must not exceed 235 mm				O-ring to probe tip	
				Print/lit.	Actual
Probe	Part number	Diameter	Thread type	Length	Length
AppliSens DO	Z010023525	12 mm (0.47 in.)	13.5 PG	235 mm (9.25 in.)	235 mm (9.25 in.)
AppliSens pH	Z001023551	12 mm (0.47 in.)	13.5 PG	235 mm (9.25 in.)	235 mm (9.25 in.)
Mettler Toledo DO	InPRO 6800/12/220, PN 52200966	12 mm (0.47 in.)	13.5 PG	215 mm (8.46 in.)	215 mm (8.46 in.)
Mettler Toledo pH	405-DPAS-SC-K8S/225, PN 104054481IG	12 mm (0.47 in.)	13.5 PG	195 mm (7.67 in.)	219 mm (8.62 in.)
Broadley-James DO	D140-B220-PT-D9	12 mm (0.47 in.)	13.5 PG	215 mm (8.46 in.)	214 mm (8.42 in.)
Broadley-James pH	F-635-B225-DH	12 mm (0.47 in.)	13.5 PG	225 mm (8.85 in.)	219 mm (8.62 in.)
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 the probe manufacturer's website for appropriate probe cable connection and part number.

1.3.2. Controllers

Thermo Scientific products are designed with an open-architecture approach to the integration of controls. Our industry-leading S.U.B. has been integrated with most controllers on the market, allowing customers to choose the control system they want, or to reduce expense by integrating with a controller that is already onsite. In order to facilitate integration, electrical schematics are provided in the ETP supplied with the HyPerforma S.U.B. Companies that offer control solutions in either current Good Manufacturing Practices (cGMP) format or non-cGMP format for Thermo Scientific S.U.B. units are listed below.

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

The HyPerforma 5.1 S.U.B. is also available as a complete turnkey system through Thermo Fisher Scientific. These S.U.B. units may be provided with integrated controls, pump towers, a control monitor, and advanced features such as data logging, multiple S.U.B. connections, and optional 21CFR part 11 compliance for cGMP manufacturing. A variety of single-use sensors are available for pH, DO, and pressure control. Thermo Fisher Scientific can provide complete, integrated solutions using the manufacturers listed below.

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

Contact your local sales representative for more information.

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

1.4. BPC characteristics

1.4.1. S.U.B. BPC components

Figure 1.24 illustrates the components of a standard 5.1 500 L BPC. Some components vary between 50–250 L and 500–2,000 L systems; see Table 1.3 on the following page for more information.

Note: 2,000 L BPCs may also have an optional condenser system.

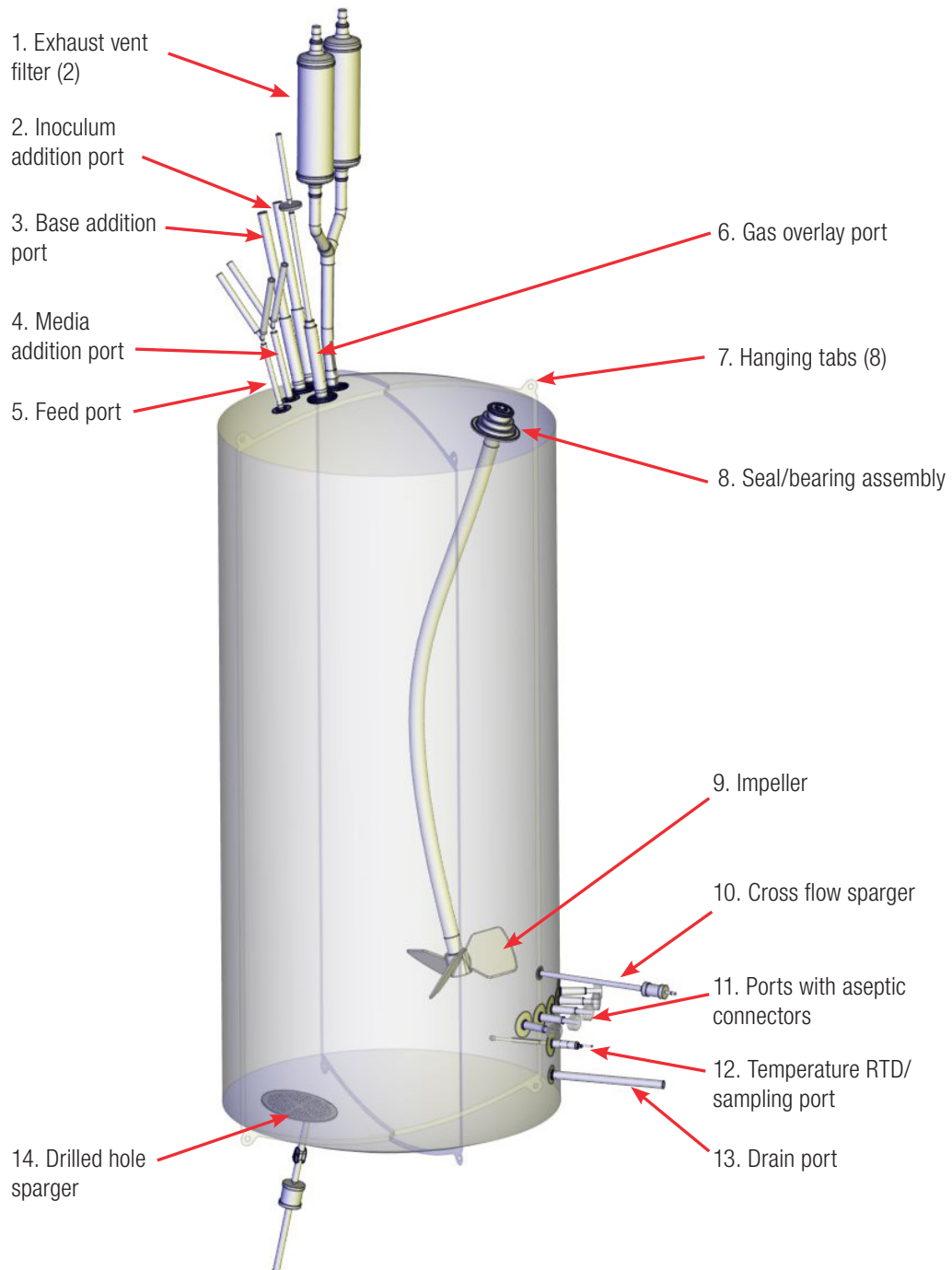


Figure 1.24. Typical 500 L BPC.

Table 1.3. BPC information for Figure 1.24.

Component	Description
1. Exhaust vent filter	Single-use capsule filter for exhaust gas exchange; 50 L, 100 L, and 250 L units have one filter, and 500 L, 1,000 L, and 2,000 L units have two filters
2. Inoculum addition port	For inoculum addition
3. Base addition port	For base addition
4. Media addition port	For addition of media
5. Feed port	For addition of other liquids
6. Gas overlay port	For the introduction of air or other gases; protected by gas filter
7. Hanging tabs (8)	For securing BPC inside the S.U.B.
8. Seal/bearing assembly	Links with the mixer motor and allows the impeller to turn while retaining integrity of the S.U.B. BPC
9. Impeller	Injection molded plastic; Links to seal/bearing assembly by C-Flex tubing
10. Cross flow sparger	Supplies oxygen during low-volume mixing
11. Ports with aseptic connectors	For integration of standard 12 mm (0.47 in.) monitoring pH and DO probes
12. Temperature RTD/sampling port	For integration of the temperature probe while retaining integrity of the S.U.B. BPC/needleless sampling or connection to the sampling manifold
13. Drain port	Used when draining the S.U.B.
14. Drilled hole sparger*	For the introduction of air, oxygen or other gases; integrated into the chamber and protected by gas filters
*Note: 2,000 L BPCs have two drilled hole spargers.	

1.4.2. S.U.B. BPC features

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

Spargers

The standard 5.1 BPC is designed with special spargers (drilled hole, cross flow, and overlay) that produce very efficient mass transfer of oxygen. They typically require much less gas inflow than conventional spargers. Gas flow rates supplied as overlay or through the cross flow sparger should also be reduced as much as possible; this will minimize both liquid evaporation and demand on the exhaust filter. Minimizing gas flow through the drilled hole sparger reduces the occurrence of foam in the headspace that may plug the exhaust filter. For more information, refer to section 3.1.3—Operating Pressure, and section 3.6—Cell culture operating instructions, in this user's guide.

Exhaust vent filter

The exhaust vent filter used on 50–1,000 L S.U.B.s is a Pall™ KA3 series filter utilizing hydrophobic PVDF membranes. To maintain a sterile connection, the standard BPC is supplied with the filter arrow pointing toward the BPC. This ensures that the filter vents are outside of the sterile connection. For users with more demanding applications, an optional vent filter heater can be used.

The exhaust vent filters used on 2,000 L S.U.B.s are Meissner™ UltraCap™ series filters utilizing hydrophobic PVDF membranes. These filters are provided in normal orientation with the flow arrow on the filter housing pointing away from the BPC. The normal orientation provides maximum filter capacity. No side vents are provided. Condensate must be managed by use of the condenser system or vent filter heater.

Connections

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

Sampling port

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

2

Hardware assembly and setup

Chapter contents

- 2.1 Initial installation preparation
- 2.2 Installation and setup

2.1. Initial installation preparation

2.1.1. Hardware shipment and setup

The Single-Use Bioreactor (S.U.B.) hardware will arrive crated. For unpacking instructions and detailed contents of the crate, please refer to the Thermo Scientific HyPerforma 5.1 S.U.B. Packing and Unpacking Guide (DOC0033), and the packaging drawings, which are included in the shipping crate. Be sure to follow the unpacking instructions provided and retain all packaging materials.

2.1.2. Hardware uncrating

The S.U.B. 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)

Detailed instructions for crating, uncrating, and assembly of 50 L, 100 L, 250 L, 500 L, 1,000 L, and 2,000 L S.U.B. units are included in the Thermo Scientific HyPerforma 5.1 S.U.B. Packing and Unpacking Guide (DOC0033). After uncrating, contact your sales representative immediately if any damage has occurred.

2.1.3. Site preparation

Electrical connections for units with AC motors and an electrical control panel

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

Electrical connections for 50 L, 100 L, 250 L, and 500 L systems with DC motors

S.U.B. units using DC motors are not supplied with electrical control panels (E-Boxes). When using a DC motor, electrical connections must be supplied by a third-party integrator.

Outer support container preparation

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



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

Electrical preparation for 50–2,000 L systems with AC motors and E-Boxes

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

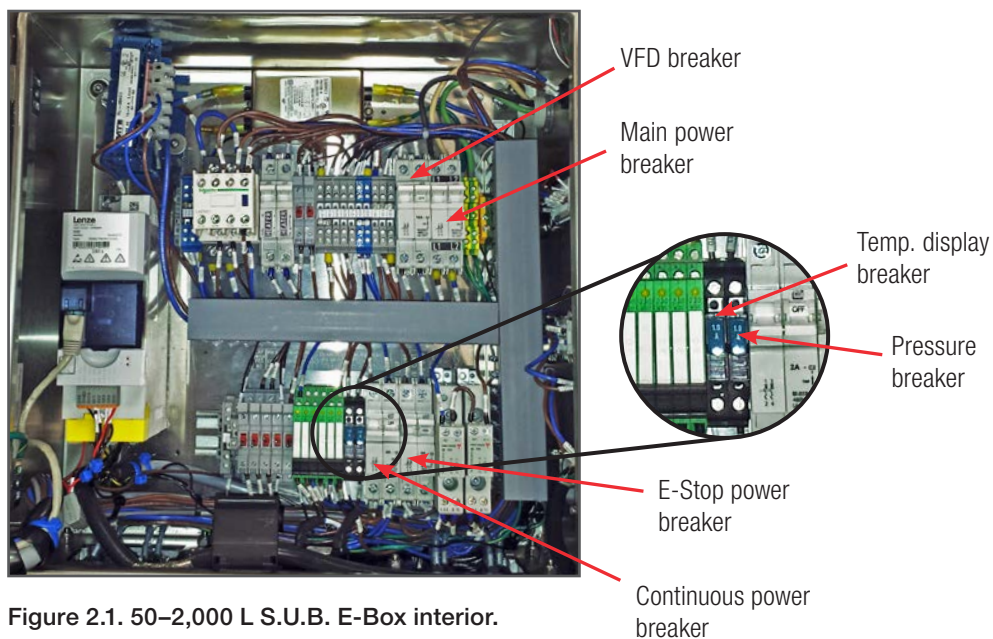


Figure 2.1. 50–2,000 L S.U.B. E-Box interior.

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

2.2. Installation and setup

2.2.1. Preparing load cells

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

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

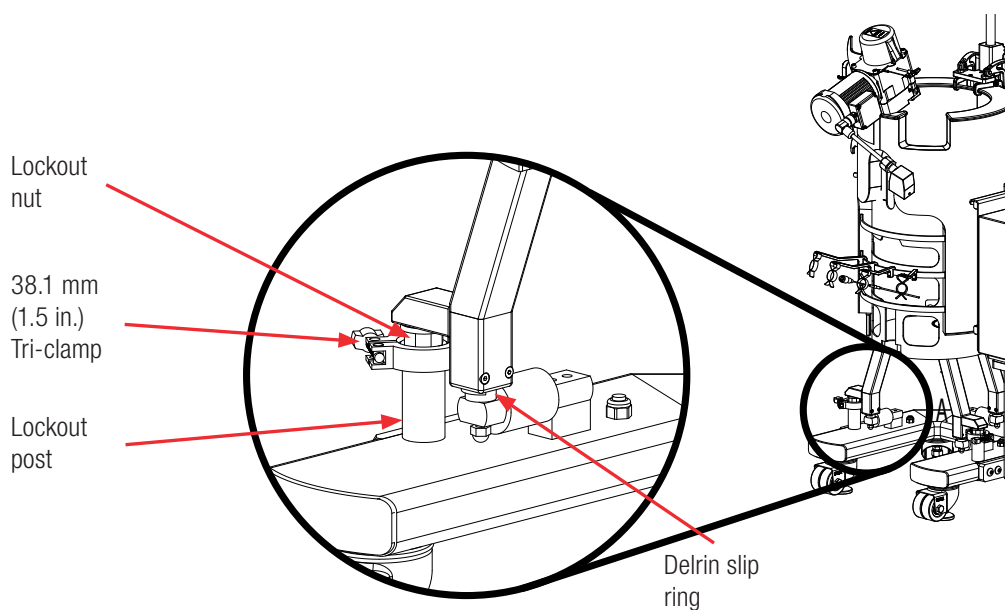


Figure 2.2. Close up view of load cells.

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

- To unlock the load cells, remove and discard the delrin slip ring if it is present. Remove the tri-clamp. Loosen the lockout nut, using the small end of the supplied tool (Figure 2.3), until the nut is tight against the base or leg of the S.U.B. Repeat this process for each load cell until all of the lockout nuts are disengaged from the lockout posts. Do not reinstall the tri-clamp.

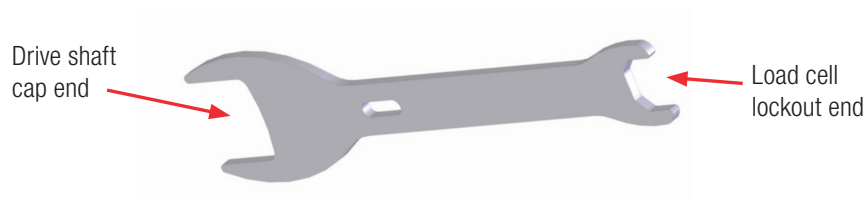


Figure 2.3. Supplied wrench.

- At this point, the S.U.B. hardware is ready to be prepared for a cell culture run.
- For systems with load cell display screens, refer to Appendix B for information about calibrating load cells.

CAUTION: Do not move the unit (especially when filled) while load cells are unlocked, as this can damage the load cells.

- 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.

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

2.2.2. Leveling and connecting the system

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

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

2. Locate the outer support container in the area for the cell culture run.
3. When monitoring the batch volume, the unit may be placed on a weight scale if load cells are not part of the system. Other methods may be used to measure all incoming and outgoing liquids.
4. Level the platform by disabling the swivel casters on the bottom of the outer support container. This is accomplished by threading the leveling feet (at the center of each caster) to the floor.
5. Verify the location of the pH/DO controllers and assure that the cable and tubing lengths are sufficient.



WARNING: Risk of electrical shock.

6. Verify that the main power is off and the emergency stop 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 250 L S.U.B.s should be connected to a dedicated 20 A circuit. Refer to hardware/electrical labels and schematics to ensure proper electrical voltage is connected to the S.U.B. The main power switch can now be turned on.
9. **For 1,000 L units only:** the water jacket ports are removed for shipping. Attach the ports to the S.U.B. using the tri-clamps provided (Figure 2.4).



Figure 2.4. Attaching water jacket port using tri-clamp.

10. Connect water inlet and outlet lines from the temperature control unit quick-connects to the jacket (Figure 2.5). For 50 L, 100 L, 250 L, 500 L, and 2,000 L units, the inlet is typically on the left side if you are facing the connectors. For the 1,000 L S.U.B. unit, the inlet is the lower connection, and the outlet is the upper.

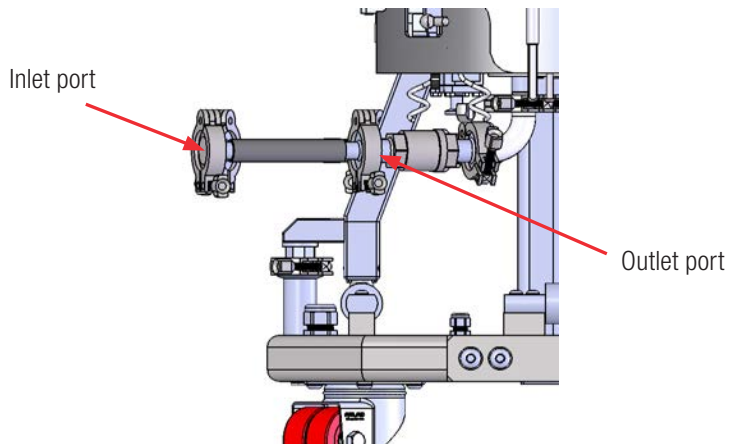


Figure 2.5. Inlet and outlet ports.

11. Insert the sparge line support (Figure 2.6) into the bottom of the S.U.B. unit, directly below where the sparger will be placed. This piece holds the sparge line vertically for maximum effectiveness. The sparge line can be wound through the coil of the holder to keep the sparger oriented properly.



Figure 2.6. Sparge line support.

2.2.3. Verifying drive shaft segments for 2,000 L systems

The 2,000 L S.U.B. is supplied with a special drive shaft that differs in appearance and material when compared to the metallic shafts used in smaller S.U.B. sizes. Due to the higher mechanical stress generated in 2,000 L S.U.B.s, these systems require drive shafts made of carbon fiber composites to reduce the weight of the long shaft.

Note: Always maintain a log history of the drive shaft and confirm that it has sufficient life remaining. **For warranty purposes, users must show documentation of proper drive shaft use.** A sample log for documenting drive shaft use is provided in Appendix D of this publication. If the age or history of a drive shaft is questionable, it should be discarded.

2.2.4. Setting the air pressure rate for motor lift adjustment (1,000 L and 2,000 L systems only)

The air pressure rate must be set before using the handheld controller for motor lifts on 1,000 L and 2,000 L systems (see section 2.2.5). The pressure regulator located on the back of the outer support container (Figure 2.7) maintains the level of air pressure used to adjust the motor lift.



Figure 2.7. Pressure regulator.

Hook up the pressure regulator to an air source and turn on the air. Increase or decrease the air supply until the air pressure rate is at 90 psi.



WARNING: Air pressure for adjusting the motor lift on 1,000 L and 2,000 L systems must stay at or below 90 psi. Air pressure above 90 psi may cause damage to the hardware.

2.2.5. Using the handheld controller for motor lifts (1,000 L and 2,000 L systems only)

The motor lift on 1,000 L and 2,000 L systems is operated by a handheld controller (Figure 2.8), which is located on a bracket attached to the front of the S.U.B. Before use, refer to section 2.2.4 to ensure that the air pressure rate is properly set.



Figure 2.8. Handheld controller for motor lifts.



WARNING: Rotating and moving parts, such as the motor lift for 1,000 L and 2,000 L systems, can cause injury. Keep hands away from moving parts during operation. Do not operate this equipment unless the supplied guarding is in place and properly functioning. It is the responsibility of the end user to assess this equipment and ensure that equipment and safeguards are in good working condition. All operators must be trained and aware of entanglement and pinch hazards and associated protective devices, such as hazard signs and guarding.

Use the following instructions to change the motor position by operating the handheld controller.

1. Before adjusting the motor lift, verify that the motor cap is closed. If the cap is open, the motor will not run. The red status sensor on the motor cap (Figure 2.9) communicates to the handheld controller if the cap is open or closed.

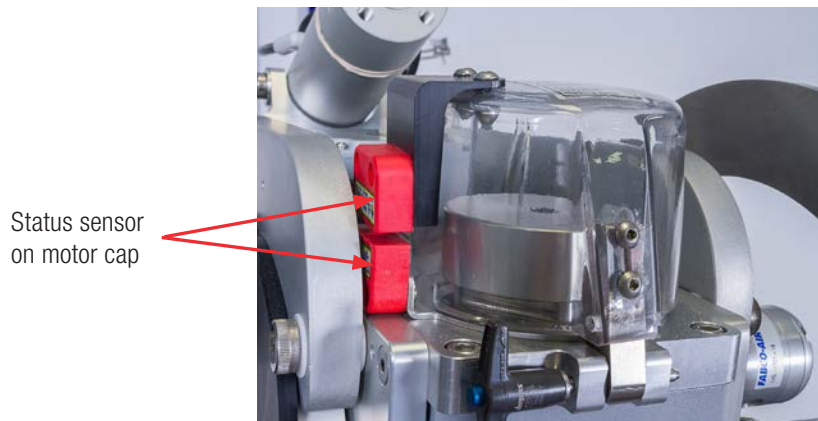


Figure 2.9. Red status sensor on motor cap.

2. Hold down the unlock/move button on the handheld controller to unlock the motor. The "unlocked" indicator on the handheld controller will be lit orange (Figure 2.8). While holding down the unlock/move button, turn the position dial to the left to lower the motor position, or to the right to raise the motor position.

Note: The motor must be in either the "up" or "down" position. If the motor is not in either position, the "intermediate position" indicator will be lit red as a warning (Figure 2.8).

3. After the motor angle is in either the "up" or "down" position, release the unlock/move button to lock the pin located on the side of the motor. The "locked" indicator will be lit green.

Important notes:

- Prior to BPC loading, the motor should be in the "up" position.
- After the BPC has been loaded and filled with air, the motor should be moved to the "down" position.
- To stop the handheld controller and movement of the motor lift in the case of an emergency, use the red Emergency Stop (E-Stop) button on the top of the handheld controller.

3

Operating information

Chapter contents

- 3.1 General system operating information
- 3.2 BPC and drive shaft loading instructions for 50 L, 100 L, and 250 L systems
- 3.3 BPC and drive shaft loading instructions for 500 L and 1,000 L systems
- 3.4 BPC and drive shaft loading, and condenser system setup instructions for 2,000 L systems
- 3.5 Probe preparation and insertion
- 3.6 Cell culture operating instructions
- 3.7 Verification procedures

3.1. General system operating information

3.1.1. BPC preparation

Each outer support container is designed for a specific BPC. Confirm that the correct volume and type of BPC is being used for the corresponding volume outer support container. 50–500 L 5.1 BPCs are different than 2.1 BPCs, and are labeled for 5:1 mixing. Sections 3.2, 3.3, and 3.4 cover the installation and setup of BPCs. Follow these instructions in the order in which they are presented.

3.1.2. BPC handling instructions

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

3.1.3. BPC operating information

Working volume

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

Note: Actual working volumes should not exceed the indicated rated working volumes by more than 10%. In addition, working volumes less than 20% of the rated volume can result in damage to the BPC and/or the S.U.B. hardware.

Operating pressure

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



WARNING: The BPC is not rated as a pressure vessel. Gas pressure within the BPC headspace should not exceed 0.03 bar (0.5 psi) at any time. Pressure above 0.03 bar (0.5 psi) may result in BPC damage or personal injury.

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

Aeration

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

A cross flow sparging strategy disrupts the dense carbon dioxide blanket at the bottom of the BPC headspace, which lets users take advantage of low-volume mixing without compromising cell cultures. This strategy requires temporarily rerouting the overlay sparger to a cross flow port near the surface of the liquid when operating at 20% working volume. When the volume is increased above 20%, the sparge line should be returned to the standard overlay port to reduce carbon dioxide in the headspace, and a single drilled hole sparger is the main source of aeration.

For more information about possible sparging strategies, review the test data in the Thermo Scientific HyPerforma 5.1 S.U.B. Validation Guide (DOC0023).

Aseptic connections

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

Draining and harvest

The S.U.B. is equipped with a bottom drain line that allows for liquid harvest by means of peristaltic pump. Connection of the bottom drain line can be accomplished by use of a tubing welder or the fitting that is provided. The bottom drain exits the BPC at the lowest vertical position on the side of the S.U.B. This allows for easy access for the user and minimizes the accumulation of cells in the area of the drain during the cell culture run. Manipulation of the BPC as the last few liters of media drain will minimize liquid hold-up within the S.U.B. The 2,000 L S.U.B. is provided with a 25.4 mm (1 in.) bottom drain near the center line of the tank bottom.

3.1.4. Hardware operating information

Heating performance

Heating times for 5.1 S.U.B. systems vary based on liquid volume and temperature, ambient or heating liquid temperature, sparging rate, and mixing rate. For heating times, see Table 3.1.



WARNING: Do not heat the system if the BPC is not at 20% liquid volume or greater. Batch temperature should not exceed 40°C.

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

System	Liquid batch volume (20% / 100%)	Initial liquid	Liquid target	Time (20% / 100%)
50 L	10 L/50 L	5°C	37°C	1 hr/1.1 hr
100 L	20 L/100 L	5°C	37°C	0.9 hr/1.6 hr
250 L	50 L/250 L	5°C	37°C	1.1 hr/3.4 hr
500 L	100 L/500 L	5°C	37°C	1.1 hr/2.2 hr
1,000 L	200 L/1,000 L	5°C	37°C	1.2 hr/4.1 hr
2,000 L	400 L/2,000 L	5°C	37°C	1.4 hr/4.0 hr

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

Protective earth grounding (units with AC motors)

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

Agitation control interface for units with AC motors and E-Box enclosures

The agitation control interface utilizes a digital display to indicate stirring speed in units of revolutions per minute (rpm). Power is supplied to the motor by a two-position power switch that is illuminated in green when turned to the "on" position (right position). The agitation should not be operated at volumes less than 20%. Stirring speed is adjusted using the up and down arrows on the agitation keypad interface on the E-Box, or using the settings on an integrated third-party controller. Due to the auto-restart capabilities of the S.U.B., the green start button on the keypad has been disabled; however, the red stop button on the keypad is active.

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

Circuit protection (units with AC motors)

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

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

Electrical breaker notes:

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

Scales and weighing systems

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

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

Refer to Appendix B for load cell display calibration instructions.

Ensure that load cells are locked down before any movement of the S.U.B. unit.

To lock the load cells before transporting any size S.U.B., follow the steps below and refer to Figure 2.2 and Figure 2.3 in section 2.2.1.

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 the nut is hand-tightened 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 overtighten the nut.

3. Assemble a standard stainless 28.6 mm (1.5 in.) tri-clamp around the flanges.
4. Repeat steps 1 through 3 for all load cells on the S.U.B.

3.1.5. External data logging and control

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

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

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

3.2. BPC and drive shaft loading instructions for 50 L, 100 L, and 250 L systems

3.2.1. Initial BPC loading steps for 50 L, 100 L, and 250 L systems

Each outer support container is designed for a specific BPC. Verify that the correct volume and type of BPC is being used for the corresponding volume outer support container. The BPC should have a tag on the bearing port labeled "5:1 Mixing." Use the following steps to install and set up the BPC.

1. Remove the irradiated BPC from the protective double polybags (Figure 3.1). Remove the cable ties from the drain line.
2. Load the BPC from the top into the outer support container, avoiding any sharp edges that may damage the BPC (Figure 3.2).
3. Orient the BPC with the bearing port up and toward the motor drive with the aseptic connector probe ports facing the bottom access cutout.
4. Place the bearing port into the bearing port receiver, close the door and close the clamp (Figure 3.3).



Figure 3.1. BPC removed from protective double polybags.



Figure 3.2. BPC loading.



Figure 3.3. Bearing port insertion.

5. Use the back access window to route the side and bottom ports through the opening in the outer support container (Figure 3.4).
6. Route the sparge lines, bottom drain, and sampling lines through the appropriate openings (Figures 3.5 and 3.6). **Note:** Although Figure 3.5 shows two drilled hole sparge lines, 50 L, 100 L, 250 L, 500 L, and 1,000 L standard 5.1 BPCs only have one drilled hole sparge line.
7. Route the sparge lines through the bottom plate and loop them around the sparge line holder (Figure 3.5).



Figure 3.4. Bottom line access.



Figure 3.5. Sparge line setup.



Figure 3.6. Drain line and port setup.

8. If a cable management system is available (see system shown in Figure 3.7), attach the lines to the appropriate inlet ports (Figure 3.8).



Figure 3.7. Cable management system in use.



Figure 3.8. Incoming line connection to inlet ports.

9. Connect the incoming gas feed lines to both the overlay filter and the sparger filter. Ensure that the filters are located above the maximum liquid level (Figure 3.9).



Figure 3.9. Inserting lines into the cable management system channels.

10. Inflate the BPC with air through the overlay filter, but do not exceed 25 slpm or 0.034 bar (0.5 psi) internal BPC pressure. Inflation time is approximately 10–20 minutes. Time will vary based on flow rate, inlet pressure, and container volume. As the BPC inflates, ensure that the ports, drain, and sparge lines are properly oriented in the support container.



WARNING: The BPC is not rated as a pressure vessel. The BPC should not be allowed to become tight during inflation or operation. DO NOT EXCEED 0.034 bar (0.5 psi) within the BPC or the BPC could fail. For reference, the BPC will appear to be tight at 0.007 bar (0.1 psi). See Table 3.7 in section 3.6.8 for recommended air flow rates. The operating pressures at the level of the S.U.B. are of primary importance and these values must be adhered to.

11. As the container fills with air, check to make sure the sparge lines are properly aligned. **Note:** Standard 5.1 S.U.B.s only use one sparge line.

Sparge line note: While a sparge line check valve is provided for each sparge line, it is not uncommon for some fluid to bypass check valves during typical use. Elevating the filter will reduce the chance that the filter is exposed to liquid.

12. Use the four bottom cutouts located at the base of the support container as a reference to align the hanging tabs on the BPC (Figure 3.10).



Figure 3.10. Hanging tab and hook.

13. Attach the bottom corners of the BPC's hanging tabs to the tab holders (pins) on the S.U.B. (Figure 3.11). The number of hanging tabs varies from two to four, according to the vessel size. **Note:** For 250 L BPCs, attach all hanging tabs to help position the ports.



Figure 3.11. Attaching hanging tab.

14. Position the bottom side drain, pulling out and downward to position the port toward the bottom edge of the S.U.B.
15. Align the row of probe ports within the access window (Figure 3.12). **Note:** Verify all port clamps are closed and located as close as possible to the body of the BPC.



Figure 3.12. Aseptic connector alignment.

16. Connect the media ground clip to the stainless steel insert in the sample line on the BPC. This step grounds the media inside the BPC and helps to eliminate electrostatic charge (Figure 3.13).

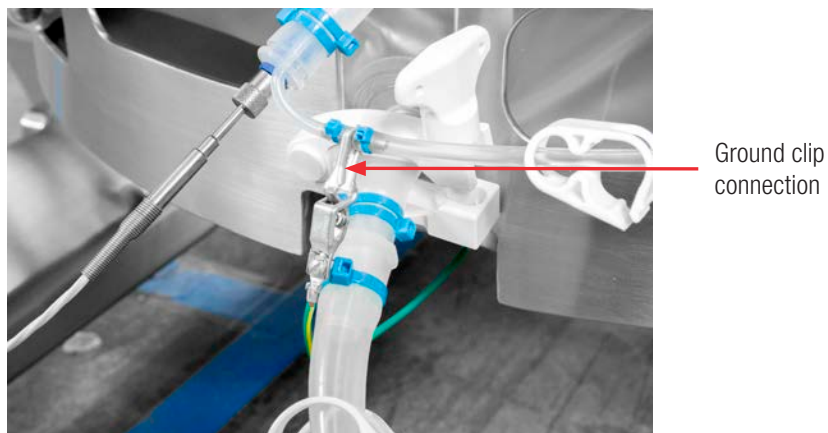


Figure 3.13. Media ground clip connection.

3.2.2. Drive shaft insertion for 50 L, 100 L, and 250 L systems



WARNING: Before you insert the drive shaft, the BPC must be adequately inflated so that it is sitting upright in the outer support container.

Figure 3.14 illustrates the components of the motor and mixing assembly. The parts labeled on the figure will be referenced throughout the drive shaft insertion process. Use the steps on the following pages to insert the drive shaft.

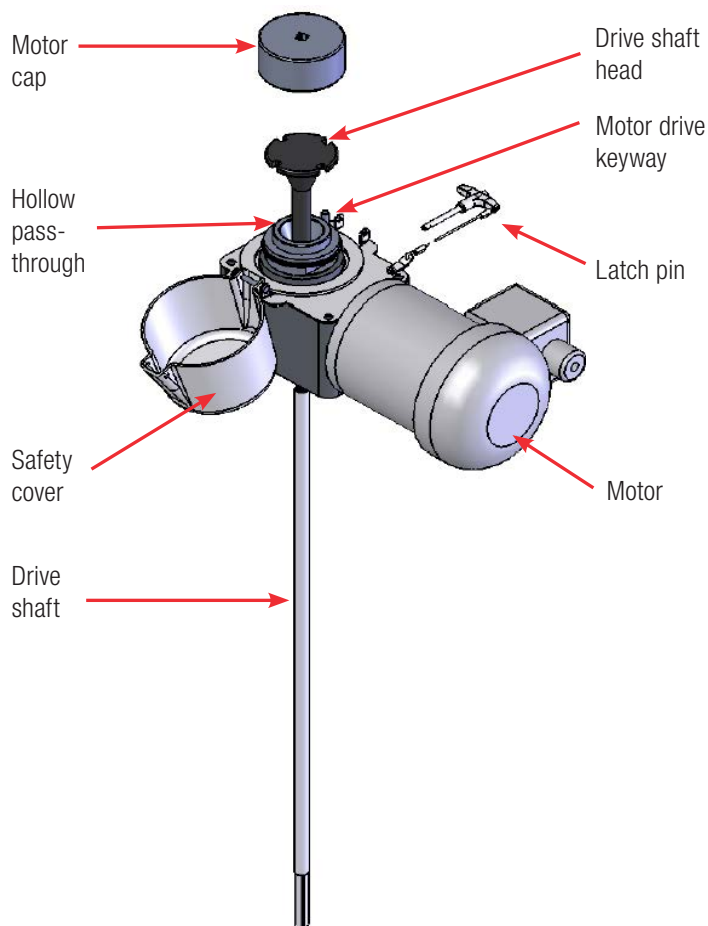


Figure 3.14. Motor and mixing assembly.

1. Remove the latch pin from the safety cover over the mixing assembly and open the cover. Unscrew the motor cap covering the hollow pass-through of the motor (Figure 3.15).



Figure 3.15. Removing the motor cap.



WARNING: Ensure that the correct drive shaft is being used. Because the 5.1 S.U.B. is capable of mixing at much lower volumes than traditional 2.1 S.U.B.s, it is important to use the correct drive shaft to avoid damaging the hardware. 50–500 L 5.1 drive shaft heads are black and engraved with "5:1 Mixing." 2:1 mixing uses a system with a different impeller angle, and is covered in a separate S.U.B. user's guide.

2. Insert the drive shaft through the hollow pass-through of the motor assembly in the following manner (Figures 3.16–3.19).
 - 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 avoid stretching the impeller tubing (Figures 3.16 and 3.17). **Do not push the drive shaft straight in.**



Figure 3.16. Loading drive shaft.



Figure 3.17. Twisting drive shaft to aid insertion.

- When approximately 50.8–76.2 mm (2–3 in.) of the shaft remains, twist back and forth slightly to engage the impeller (Figure 3.18).
- When approximately 25.4–50.8 mm (1–2 in.) of the shaft remains, twist back and forth slightly to engage the bearing assembly.
- When approximately 6.4 mm (0.25 in.) of the shaft remains, twist to align the motor drive keyway with one of the four outer slots on the drive shaft head (Figure 3.19).



Figure 3.18. Preparing to engage impeller.



Figure 3.19. Drive shaft head aligned.

3. Directly couple the drive shaft to the motor drive (Figures 3.20–3.22).
 - Place the motor cap on the hollow pass-through and hand-tighten clockwise (Figure 3.20).



Figure 3.20. Replacing motor cap.

- Tighten the motor cap by placing a spanner wrench on the hollow pass-through and tighten the motor cap using the supplied torque wrench (Figure 3.21). **Wrench 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 3.21. Tightening cap.

- Remove the wrenches from the system and place in the storage holders.
- Close the safety access cover and insert the latch pin (Figure 3.22).



Figure 3.22. Replacing and latching cover.

3.2.3. Final installation steps for 50 L, 100 L, and 250 L systems

1. The air supply to the overlay can be turned off once the drive shaft has been inserted.
2. Optional: Wrap and secure the vent filter heater on the exhaust filter. 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. The controller is preset to 50°C.
3. Secure the exhaust vent filter on its holder (Figure 3.23).
Note: Some custom BPCs are supplied with dual exhaust vents. The vent bracket can accommodate 10 in. and 4 in. filters in either single or dual configuration.



Figure 3.23. Vent filter installation.

4. Attach the overlay sparge line and any other lines to the cable management system, if available (Figure 3.24).



Figure 3.24. Optional cable management system on a S.U.B. unit.

5. 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. Bar clamp installation.

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

7. Insert the RTD or selected temperature sensor into the thermowell (Figures 3.26 and 3.27).
 - Place a small amount of glycerol (0.5 mL) in the well to aid in heat transfer. The glycerol also acts as a lubricant, which helps with probe insertion.
 - The sensor should be inserted until the base of the probe meets the mouth of the thermowell. Rotate the probe either clockwise or counterclockwise to aid insertion.
 - Secure by twisting the luer lock collar, if provided. The thermowell will stretch slightly when the RTD is seated.



Figure 3.26. Sensor insertion.



Figure 3.27. Securing sensor.

8. Optional: Connect a pressure sensor to the CPC aseptic connector at the top of the BPC. Then connect the appropriate pressure transducer cable to the third-party controller.
9. Continue to section 3.5 for probe preparation and insertion instructions.

3.3. BPC and drive shaft loading instructions for 500 L and 1,000 L systems

3.3.1. Initial BPC loading steps for 500 L and 1,000 L systems

Note: The figures in this section feature a 500 L 5.1 S.U.B. Please note that 1,000 L 5.1 S.U.B.s have a motor that can be operated in two positions. The motor must be in the "up" position to load the BPC into 1,000 L S.U.B.s.

Checkpoints prior to BPC loading

- ✓ The correct volume BPC is being used for the corresponding volume outer support container. 500 L 5.1 BPCs should have a tag on the bearing port labeled "5:1 Mixing."
- ✓ The outer support container is stationary with the casters locked into place. BPC loading may require operators to step inside the bioreactor, and the unit must be stationary for the safety of both the operator and equipment.
- ✓ Two operators are available for ease in BPC loading.
- ✓ A ladder or other means of elevation is available for drive shaft insertion.
- ✓ The motor is in the "up" position (1,000 L systems only). See section 2.2.5 for instructions on using the handheld controller to change the position of the motor.

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

1. Open the door on the bioreactor support container and reach inside to open the clamp on the bearing port receiver located below the motor (Figures 3.28 and 3.29).



Figure 3.28. Opening the bioreactor door.



Figure 3.29. Close-up of bearing receiver clamp.

2. Remove the irradiated BPC from the protective double polybags (Figure 3.30). Do not remove the 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.
3. Reach into or step inside the outer support container with the front face (bearing port side) of the BPC oriented toward the motor (Figure 3.31).



Figure 3.30. BPC in protective polybags.



Figure 3.31. Bearing port orientation.

4. Place the top line sets, still in polybags, over the top edge of the tank (Figure 3.32). This will keep the container from being restricted during the air inflation step.



Figure 3.32. Line sets on edge of tank.

5. Load the container bearing port into the receiver (Figure 3.33). Close the door and clamp it shut (Figure 3.34).



Figure 3.33. Bearing port in receiver.



Figure 3.34. Door clamped shut.

6. Remove the bubble wrap from the sparger filters. Guide the sparge inlet lines and filters through the bottom cutouts in the outer support container (Figure 3.35). The operator can reach just below the S.U.B. to further extend the sparge lines from the cutouts (Figure 3.36).



Figure 3.35. Sparge line insertion.



Figure 3.36. Sparge line extension.

7. Pass the bagged drain line set and temperature/sampling port set through the large cutout in the front of the outer support container (Figure 3.37). Extend the drain line set through the cutout (Figure 3.38).



Figure 3.37. Drain/sampling line set insertion.



Figure 3.38. Drain/sampling line extension.

8. Connect the pressure transducer to the monitor. After the display has stabilized, tare the monitor. The monitor should be allowed to warm up for 30 minutes before taring. Verify that the monitor reads zero.
9. The BPC must be partially inflated until it is sitting upright. This allows proper insertion of the drive shaft and aids in the proper alignment of the BPC in the outer support container.
 - Attach the air supply to the overlay gas inlet line.
Note: Air pressure to the overlay gas line on the S.U.B. BPC should not exceed 0.2 bar (3 psi) or 25 slpm.
 - Begin air inflation through the overlay gas line. Filling the container with air takes approximately 15–20 minutes before drive shaft insertion can begin. Times will vary based upon flow rate and inlet pressure.
 - Steps 10–13 can be completed while the BPC is filling with air.



WARNING: The BPC is not rated as a pressure vessel. DO NOT EXCEED 0.034 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. See Table 3.7 in section 3.6.8 for recommended air flow rates. The operating pressures at the level of the S.U.B. are of primary importance and these values must be adhered to.

10. Attach the incoming gas supply to the sparger gas inlet line.
Note: Air pressure to the sparger on the BPC should not exceed 0.55 bar (8 psi). Also, while a sparge line check valve is provided for each sparge line, some fluid may bypass check valves during typical use. Elevating the filter to ensure that it is not at the low point of the sparge line will reduce the chance that the filter is exposed to liquid.
11. Tare the load cell display before proceeding.
12. Attach all of the hanging tabs on the BPC to the hooks on the bottom of the outer support container to help position the ports (Figures 3.39 and 3.40). Verify that the sparger filter and spargers remain in the correct position. It is recommended that users secure the hanging tabs on the front BPC panel first. This way the door will not be an obstruction when connecting the last set of hooks.



Figure 3.39. Hanging tab and hook.



Figure 3.40. Attaching tab.

13. Remove the protective packaging from the exhaust vent filters (Figure 3.41).



Figure 3.41. Removing protective packaging.

14. If you are using a 1,000 L system, move the motor into the "down" position using the handheld controller after the BPC has filled with air. See section 2.2.5 of this manual for detailed instructions for using the handheld controller.

3.3.2. Drive shaft insertion for 500 L and 1,000 L systems

The drive shaft is constructed in multiple segments, which must be assembled and inserted in pieces. Operators should be elevated (i.e. ladder) to effectively assemble and insert the drive shaft.

CAUTION: Review ceiling height requirements in Chapter 4 of this user's guide before trying to insert the drive shaft.



WARNING: Ensure that the correct drive shaft is being used for 500 L systems. Because the 5.1 S.U.B. is capable of mixing at much lower volumes than traditional 2.1 S.U.B.s, it is important to use the correct drive shaft to avoid damaging the hardware. 500 L 5.1 drive shaft heads are black and engraved with "5:1 Mixing." 2:1 mixing in 500 L S.U.B.s uses a system with a different impeller angle, and is covered in a separate S.U.B. user's guide. 1,000 L 5.1 systems use drive shafts with white heads that are NOT labeled for 5:1 mixing.

Figure 3.42 illustrates the components of the motor and mixing assembly. The parts labeled on the figure will be referenced throughout the drive shaft insertion process. Use the steps in this section to assemble and insert the drive shaft.

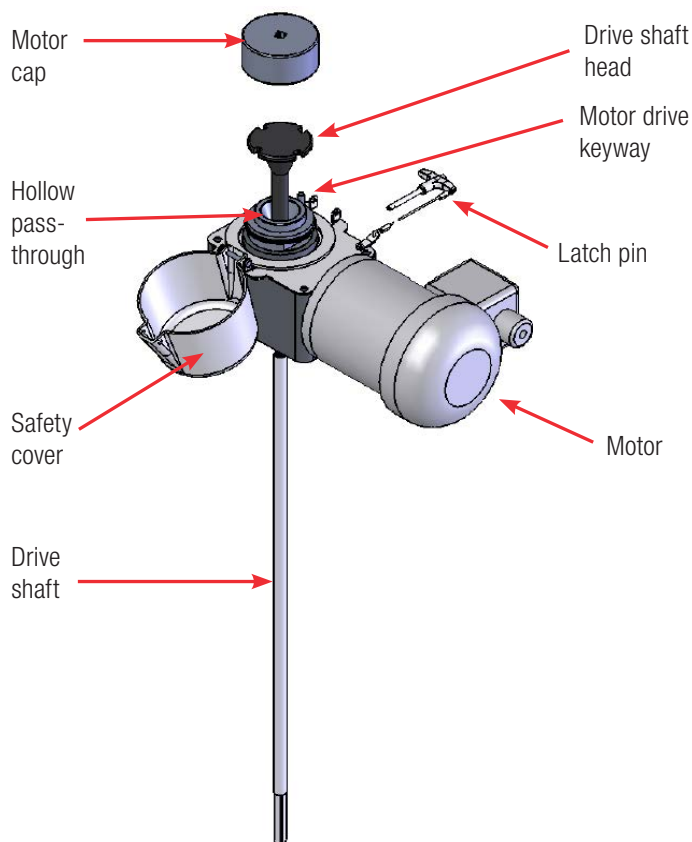


Figure 3.42. Motor and mixing assembly.

1. Prepare the hollow pass-through by first removing the latch pin on the safety cover (Figure 3.43), opening the safety cover (Figure 3.44) and removing the motor cap of the mixing assembly (Figure 3.45).



Figure 3.44. Opening safety cover.



Figure 3.45. Cap removal.



Figure 3.43. Latch pin removal.

2. Verify that the two, three, or four segments of the drive shaft, all with matching serial numbers, are located in the drive shaft holders on the side of the outer support container. For the three-piece drive shaft loading described here, the segments will be referred to as upper (the segment with the drive shaft head), middle (the segment with the internal/external threads on each end), and lower (the segment with the square end). For 1,000 L systems, lubricate the threaded ends with a light coat of food-grade anti-seize with each use. **Always verify that the drive shaft segments have matching serial numbers prior to assembly and use.**

3. First, insert the lower segment through the hollow pass-through of the mixer drive (Figure 3.46). Slide the latch pin from the motor assembly into the shaft to prevent it from falling into the tube (Figure 3.47). Assemble the middle and lower segments of the drive shaft by joining them with a twisting motion, fastening the two segments together (Figure 3.48).

Note: Segmented shafts are left-threaded (reverse-threaded) to avoid loosening during operation.



Figure 3.46. Inserting lower section.



Figure 3.47. Latch pin in shaft.



Figure 3.48. Segment assembly.

4. Place one wrench on the flat area in the middle drive shaft segment and another wrench on the lower segment, then tighten the connection using a counterclockwise rotation (Figure 3.49). After the segments are secure, return the wrenches to the tool holder. **CAUTION:** Do not over-tighten; a snug fit is sufficient. Remove the latch pin.



Figure 3.49. Tightening of shaft connections.

5. Repeat the actions in steps 3 and 4 to attach the upper segment of the drive to the partially-assembled drive shaft.
6. Using two hands, carefully guide the completed drive shaft into the BPC using a slight back-and-forth twisting motion. **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 as the end of the drive shaft begins to couple with the impeller. **Do not push the drive shaft straight in.**

- When 50.8–76.2 mm (2–3 in.) of the shaft remains, twist slightly to engage the impeller (Figure 3.50).



Figure 3.50. Drive shaft insertion.

- When 25.4–50.8 mm (1–2 in.) of the shaft remains, twist slightly to engage the bearing assembly.
- When 6.35–12.7 mm (0.25–0.50 in.) of the shaft remains, twist to align the motor drive keyway with one of the four outer slots on the drive shaft head (Figure 3.51).



Figure 3.51. Drive shaft head aligned.

7. Directly couple the drive shaft to the motor by placing the motor cap back on the hollow pass-through and tighten.

8. Tighten the motor cap by placing the spanner wrench counterclockwise on the hollow pass-through and tighten using the supplied torque wrench (Figure 3.52). **Wrench 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.).



Figure 3.52. Tightening motor cap with wrenches.

9. Verify that the wrenches are removed from the system and returned to the storage holders.
10. Close the safety access cover and insert the latch pin.

3.3.3. Final installation steps for 500 L and 1,000 L systems

1. Secure the exhaust vent filters to the top-mounted holders (Figure 3.53), or if you are using elevated dual exhaust filters, use the adapter piece and extended filter bracket (Figure 3.54).

Note: 500 L BPCs and some custom BPCs are supplied with dual exhaust vents. The vent bracket can accommodate 10 in. and 4 in. filters in either single or dual configuration.



Figure 3.53. Vent filter.



Figure 3.54. Extended dual filter bracket.

2. Fully extend the drain line set through the front cutout and attach the probe shelf.
3. Remove the polybag from the drain line set and position the line clamp as close as possible to the BPC port and close. Use a cable tie around the clamp to ensure the clamp does not open.
4. Align the aseptic connector ports through the front access window (Figure 3.55).



Figure 3.55. Aseptic connector port alignment.

5. Remove the plastic insert located in the thermowell, if present.
6. Insert the RTD or another selected temperature sensor into the thermowell (Figure 3.56).
 - Place a small amount of glycerol (0.5 mL) in the thermowell to aid in heat transfer. The glycerol also serves as a lubricant and aids in insertion.
 - The sensor should be inserted until the base of the RTD meets the mouth of the thermowell.
 - Secure by twisting the luer lock collar, if provided; the thermowell will stretch slightly when the RTD is seated (Figure 3.57).

Note: Verify that all port clamps are closed and located as close as possible to the body of the BPC.



Figure 3.56. Temperature sensor insertion.



Figure 3.57. Securing temperature sensor.

7. Optional: Connect a pressure sensor to the CPC aseptic connector at the top of the BPC. Then connect the appropriate pressure transducer cable to the third-party controller.
8. Refer to section 3.5.3 for probe insertion instructions.
9. Close the bottom access door. The proper latch tension can be obtained by a combination of feel and visual inspection. When closing the latch, the handle should begin to provide resistance to closing when the leading edge of the safety pin pass-through of the latch handle aligns with the outside edge of the latch base (Figure 3.58). **Note:** When the latch is under-tensioned, the safety pin pass-through of the latch handle will be covered within the latch base and the handle will close very easily. If the latch is over-tensioned, the handle will be excessively difficult to close.



Figure 3.58. Latching the access door.

10. The access doors must be closed and fully latched prior to filling the system with liquid.
11. Continue to section 3.5 for probe preparation and insertion instructions.

3.4. BPC and drive shaft loading, and condenser system setup instructions for 2,000 L systems

3.4.1. Initial BPC loading steps for 2,000 L systems

Checkpoints prior to BPC loading

- ✓ The correct volume BPC is being used for the corresponding volume outer support container.
- ✓ The motor is in the "up" position. For information on using the handheld controller for motor lifts, see section 2.2.5.
- ✓ The BPC lift control is plugged into a 120–240 VAC receptacle, and the Main Disconnect and Motor Enable switches on the BPC lift control are switched to "off."
- ✓ Three operators are available for ease in BPC loading.
- ✓ A ladder or other means of elevation is available for drive shaft insertion (see the specifications in Chapter 4 for system ceiling height requirements).
- ✓ The equipment has been evaluated against your confined space safety standards and procedures.

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

1. Switch on the main power to the control panel. Ensure that the drive motor is not running. Open both the front and rear doors on the outer support container.
2. Verify that the motor area is clear and the Vertical Lift switch on the BPC lift control (located on the side of the S.U.B.) is in the "up" position. Then flip the Motor Enable switch on the BPC lift control to the "on" position. The BPC lift should perform a homing operation, which fully raises the wires to the hard stop of the support arms before lowering them to the "up" position.
 - **CAUTION:** Keep hands clear during the homing operation.
 - The homing operation is complete when the lift stops moving.
3. Before lowering the BPC lift, ensure that the S.U.B. area is clear. **Do not lower the BPC lift if there are any obstructions.** Flip the Vertical Lift switch down to lower the BPC lift hooks.

- Two operators should carefully remove the irradiated BPC from the protective double polybags (Figure 3.59). Do not remove the 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 or drag on the floor.
- Load the BPC through the rear access door (Figure 3.60), orienting the bottom of the container into the door first with the bearing port facing upward. Keep the container folded as supplied in the packaging to allow the BPC to unfold naturally when it is raised by the BPC lift.



Figure 3.59. Removing the BPC from polybags.



Figure 3.60. Loading the BPC.

- Using the rear or front door for access, connect the retainer hooks on the BPC lift to the top of the BPC via two of the hanging tabs (located across from each other) (Figure 3.61).



Figure 3.61. Connecting tabs to BPC lift.

7. One operator should remain elevated to observe from above while another operator, at ground level, operates the BPC lift control. Flip the Vertical Lift switch up on the BPC lift control to raise the BPC lift hooks. **CAUTION: Do not reach into the tank during this operation.** The BPC lift should remain in the "up" position during the rest of the BPC loading process.
8. After the BPC has been lifted, hook the tabs on the bottom of the BPC to the pins on the S.U.B.
9. Use an elevated platform to open the clamp on the bearing port receiver located underneath the motor. Remove the black protective cap from the bearing port (Figure 3.62), load the BPC bearing port into the receiver (Figure 3.63), close the bearing assembly door, and latch it (Figure 3.64).



Figure 3.62. Removing the bearing port cap.



Figure 3.63. Loading the bearing port.



Figure 3.64. Closing and latching door.

10. Place the top line sets (still in polybags) over the side of the outer support container (Figure 3.65). This will help support the weight of the BPC and also keep the BPC from being restricted during the air inflation step.



Figure 3.65. Placing linesets over tank edge.

11. If your BPC includes exhaust vent filters, ensure that they are lifted through the middle of the motor lift instead of to either side. This will ensure the exhaust vent filters are properly oriented. If you are using the exhaust condenser system, follow the setup instructions in section 3.4.2 of this guide. If you are using elevated exhaust vent filters, use the corresponding extended dual vent filter bracket and filter heaters.

To load the optional exhaust vent filters, follow the steps below.

- Clip each filter one at a time into the elevated vent filter holder system (Figure 3.66). Carefully center the filter housing, allowing the clip to secure it near the hose barb connections.



Figure 3.66. Clipping filter to holder.

- Ensure that the routing of the exhaust tubing will not likely become kinked.
- Place the vent heaters around each filter (Figure 3.67), verifying that the snap retainers are secured. Position the power leads to avoid interfering with the vent holder brackets.



Figure 3.67. Installing heaters.

- Raise and rotate the vent holder bracket as needed (Figure 3.68). Make a final inspection to ensure that no kinks or low spots will occur in the tubing between the BPC and the filter, even if the BPC becomes pressurized.



Figure 3.68. Raising the vent holder bracket.

- Connect the power to the vent heaters and verify operation of the controllers.
 - Inspect the controllers' setpoints (recommended 60°C). After two to five minutes of operation, verify that the vent heaters are warm and are near the desired temperature setpoints. Verify that no alarm indicators are active.
12. Open the tubing set polybag and connect the pressure transducer to the monitor. Once the display has stabilized, tare the monitor. The monitor should be allowed to warm up for 30 minutes and the sensor connected for 10 minutes before taring. Verify that the monitor reads zero.
 13. Clamp the drilled hole sparge, exhaust, and cross flow lines so that the air supplied by the overlay gas inlet line flows directly into the BPC (Figure 3.69).



Figure 3.69. Clamping the exhaust lines prior to filling the BPC with air.

14. The BPC must be partially inflated to aid in the proper alignment of the BPC in the outer support container, and proper insertion of the drive shaft.
 - Attach the air supply to the overlay gas inlet line at the top of the BPC.
 - Begin filling the BPC with air. Operators should allow the container to fill to greater than half volume. This typically takes less than 20 minutes.
 - Steps 15–18 can be completed while the BPC is filling with air.

Note: Air pressure to the overlay gas line on the BPC should not exceed 0.344 bar (5 psi) or 100 slpm.



WARNING: The BPC is not rated as a pressure vessel. DO NOT EXCEED 0.034 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. See Table 3.7 in section 3.6.8 for recommended air flow rates. The operating pressures at the level of the S.U.B. are of primary importance and these values must be adhered to.

15. Feed the probe belt, sample line, and the subsurface addition lines through the front access door (Figure 3.70).



Figure 3.70. Feeding lines through the front access door.

16. Remove the sparge lines from the polybags and bubble wrap from the sparge filters. Use the rear door to gain inside access to the floor of the hardware. Place a clamp on the bottom drain line at this time (Figure 3.71).



Figure 3.71. Clamping bottom drain line.

17. The center insert on the tank floor provides the port locations for the bottom drain (Figure 3.72) and the gas lines for the drilled hole sparger. Guide the sparger inlet line and filter through the bottom cutout in the tank (Figure 3.73). To remove the bottom cutout, lift and rotate it in a counterclockwise direction.



Figure 3.72. Drain line support.

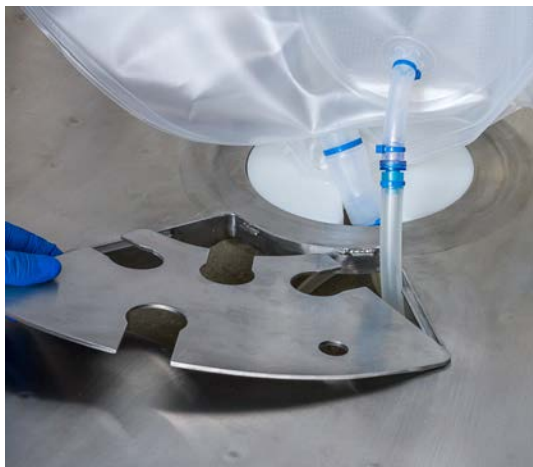


Figure 3.73. Drilled hole sparger line.

Sparge line notes:

- The plastic center tank insert also contains cutouts for porous frit sparge lines. Porous frit spargers are not available on standard 5.1 BPCs, but they are optional on custom BPCs.
- Air pressure to the spargers on the BPC should not exceed 8 psi.
- While a sparge line check valve is provided for each sparge line, it is not uncommon for some fluid to bypass check valves during typical use. We recommend elevating the sparge line filter as is feasible to help reduce this tendency.

18. Attach all of the hanging tabs to help position the ports. Using the positioning tab pins provided, secure the BPC by attaching the tabs on the bottom of the BPC onto the position tab pins (Figures 3.74 and 3.75). Verify that the sparger filter and spargers remain in position while attaching the tabs. It is recommended that users secure the tabs on the front BPC panel first. This way, the larger rear door will allow access when connecting the last set of tab pins.



Figure 3.74. Pulling the container tab toward the pin.



Figure 3.75. Securing the container tab on the pin.

19. After the BPC has filled to greater than half volume, unclamp the drilled hole, exhaust, and cross flow lines.

3.4.2. Condenser system setup for 2,000 L systems

Condenser system functional overview

The condenser system is intended to be used as an accessory for large S.U.B.s as an alternative to vent filter heaters. Condenser systems are recommended for use with 2,000 L S.U.B.s. The condenser's purpose is to prevent liquids and solids from condensing and collecting inside of the vent filters of the S.U.B. The condenser system cools the exhaust gases leaving the S.U.B. chamber, condensing the moisture out of the saturated gases coming from the S.U.B. The liquid condensate that is stripped from the exhaust gases is then pumped back into the bioprocessing container chamber, creating a sterile loop and significantly reducing liquid loss due to evaporation. The condenser plate on condenser systems with a cart assembly is chilled by a closed bath recirculating chiller, which has sufficient capacity to cool two condenser plates simultaneously. The condenser plate on side-mounted condenser systems is chilled by a house recirculating chilling loop. Figures 3.76 and 3.77 show both the cart assembly and side-mounted (2,000 L systems only) condenser system options.

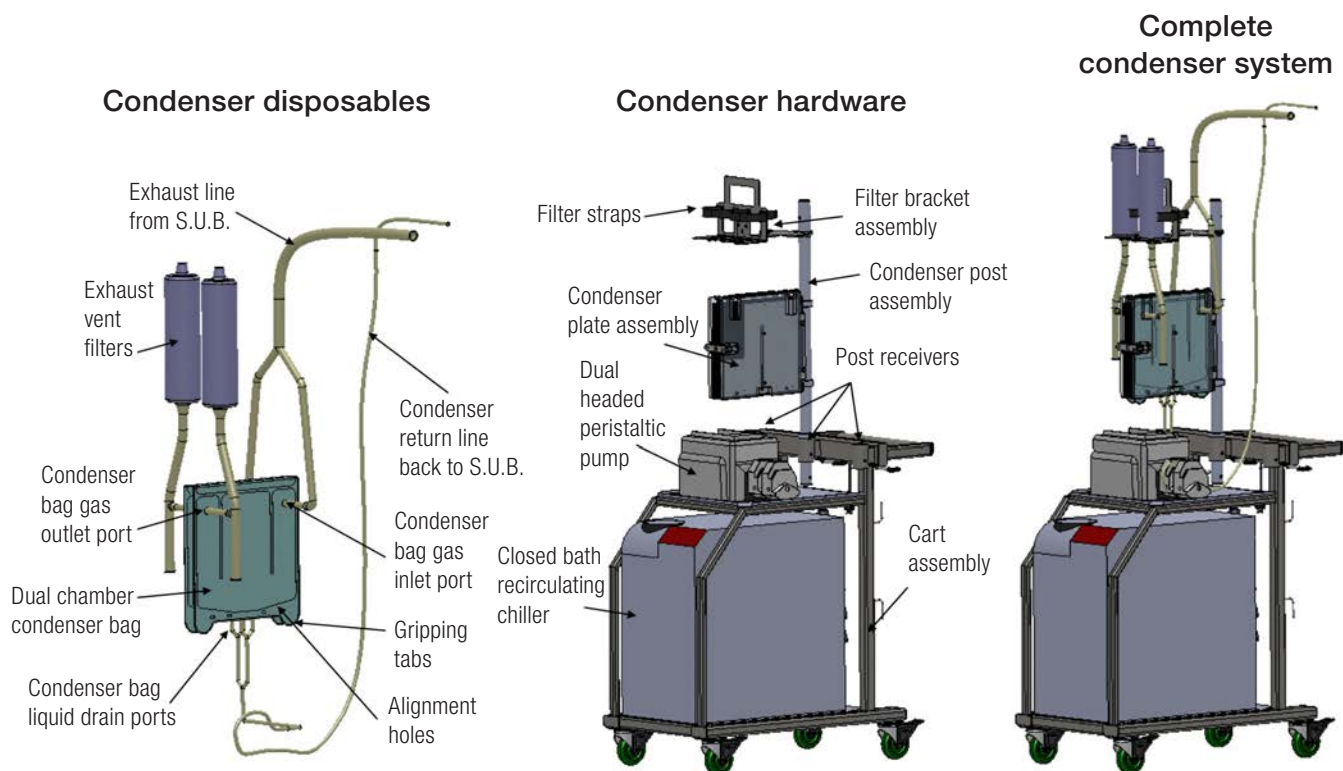


Figure 3.76. Overview of condenser system cart assembly option for 2,000 L S.U.B.s.

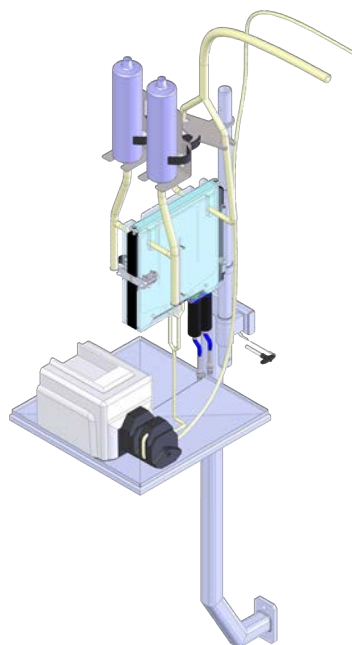


Figure 3.77. Side-mounted condenser system option for 2,000 L S.U.B.s.

When to use the condenser system

2,000 L S.U.B. BPC with single-use condenser system

Large 254 mm (10 in.) hydrophobic PVDF filters with a nominal 0.2 micron pore size were specified in order to increase the available surface area for off-gassing. In conjunction, the standard 2,000 L S.U.B. is designed for use with a single-use condenser system. This allows the S.U.B. to utilize a powerful phase-change type system which provides improved exhaust vent protection and reliability due to the ability to strip condensate and atomized materials that may be present from the off-gas stream of the S.U.B. This system has been shown to significantly reduce the “fouling” load on the vent filters that inherently increases operating back pressure as the cell culture run batch progresses. See the HyPerforma 5.1 S.U.B. Validation Guide for details.

2,000 L S.U.B. BPC with vent and heaters only

Some end users may prefer to omit the condenser system on the 2,000 L S.U.B. with the expectation that this will allow for a more uniform installation (similar to smaller S.U.B. systems used in the upstream seed train), or will perhaps reduce system complexity and cost. The use of exhaust vent heaters and 254 mm (10 in.) filters will provide impressive flow capacity over short periods (less than five days). However, the high sparge rates required during the scale-up of the S.U.B. to the 2,000 L working volume may eventually create conditions of increased operating back pressure, usually due in part to blocking of the filter media. Depending upon the application, the user has the option of using both filters in parallel or initiating the run with a single filter, temporarily clamping off the line to the other filter (it being reserved as redundant back-up).

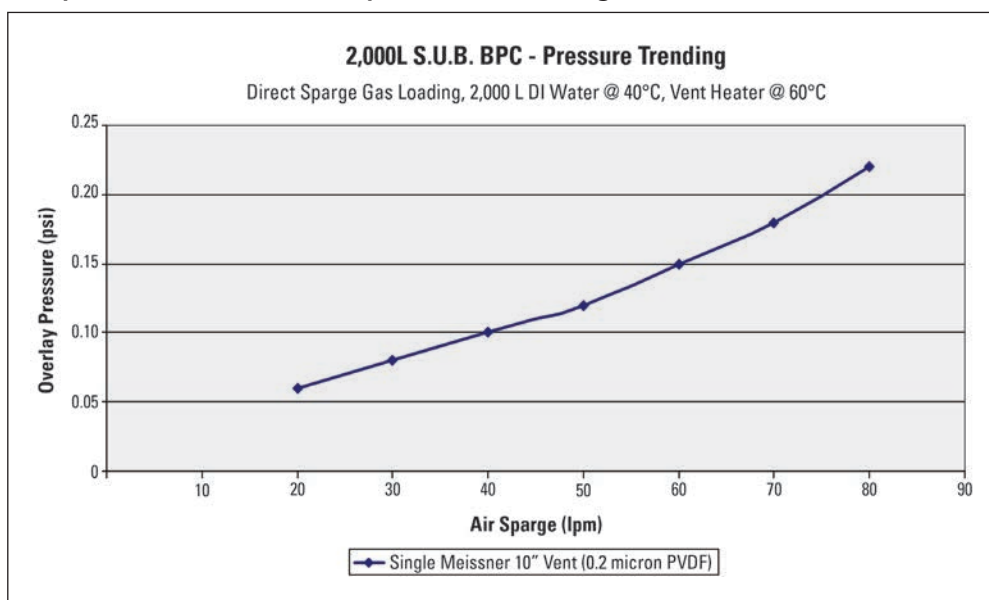
Table 3.2 may help end users specify the BPC configuration and operating parameters for custom 2,000 L S.U.B. applications when not utilizing the exhaust condenser. Because the operating parameters of different cell cultures vary widely, a safety factor should be used to temper the data. Accordingly, the data we used to generate a control base line are for reference only (filter fouling will vary and must be considered to ensure reliable performance). It is assumed no foam is present in the exhaust stream.

Table 3.2. Condenser system overview.

S.U.B. system 2 each 254 mm (10 in.) vents	Run duration	Maximum combined flow rate recommended	Resulting safety factor
2,000 L S.U.B.	7 days	40 slpm	2x
2,000 L S.U.B.	10 days	32 slpm	2.5x
2,000 L S.U.B.	14 days	27 slpm	3x
2,000 L S.U.B.	21 days	Single-use condenser strongly recommended	

The above recommendations were generated using the test conditions shown in Graph 3.1. In this case, a 2,000 L S.U.B. was filled with 2,000 liters of DI water with a batch temperature of 40°C using a MKS vent filter heater at 60°C. Safety factor estimates are based on a maximum continuous internal S.U.B. BPC pressure not to exceed 0.006 bar (0.1 psi), which corresponds to 40 slpm with a single 254 mm (10 in.) vent. **Note:** These results do not take into consideration a “fouling” safety factor.

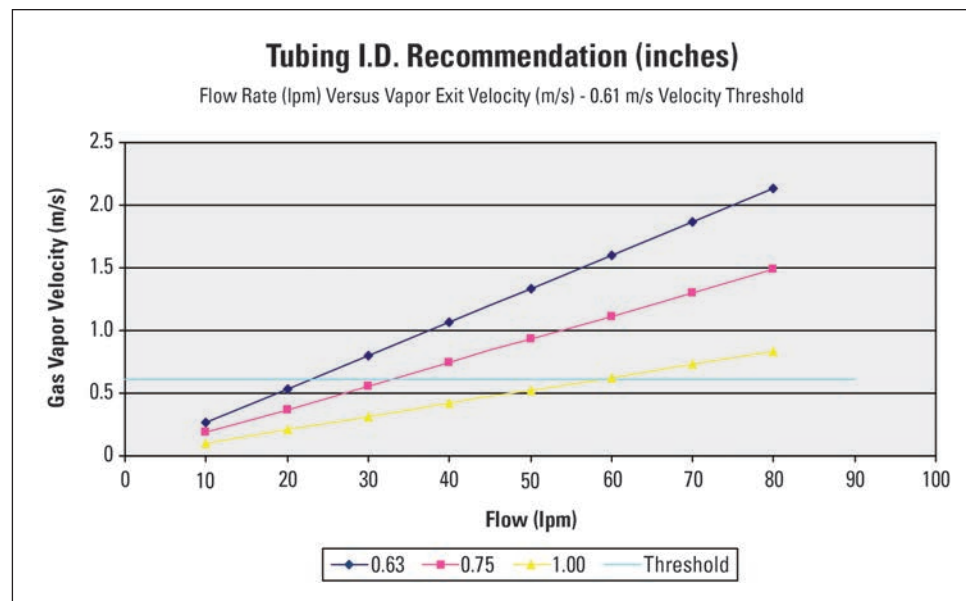
Graph 3.1. 2,000 L S.U.B. pressure trending.



Also consider the size and type of tubing used to connect the exhaust vents to the S.U.B. BPC (when not using an exhaust condenser). Braid reinforced tubing provides the best protection against kinking or accidental pinching of the exhaust line. The 254 mm (10 in.) vents are supplied with 19.1 mm (0.75 in.) hose barbs and this tubing diameter will allow condensate to return to the S.U.B. at total off-gas flow rates up to 30 slpm (assuming the tubing is near a vertical orientation). Testing has shown that large diameter tubing will allow for lower exhaust gas velocities and if the vapor velocity is below 0.6 m/s (1.96 ft./s), gravity will allow the condensate formed in the tubing to return to the batch process (Graph 3.2).

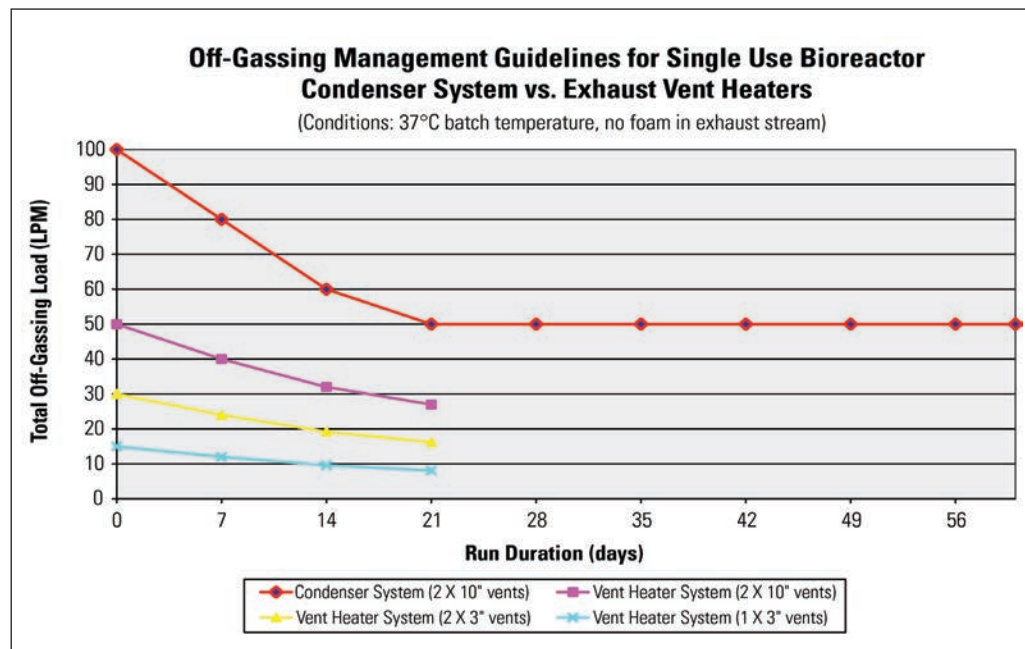
Note: Restrictive tubing connectors can create flow bottle necks and 12.7 mm (0.5 in.) inner diameter (ID) tubing is typically deemed too small for the 2,000 L S.U.B.

Graph 3.2. Tubing diameter recommendation.



Various vent filter configurations are available on the S.U.B. depending upon the process scale and intended application. Graph 3.3 provides a reference for determining the relative capacity of different filters depending upon the amount of gas flow anticipated and the length of the run. In all cases, using a vent filter heater will reduce the chance of condensate blocking the filter, but 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. In all cases, a vent filter heater has very little tolerance for handling the presence of foam in the exhaust stream. A small feed of antifoam (e.g., FoamAway™ Irradiated AOF Antifoaming Agent, catalog number A1036901) added directly to the liquid surface of the culture head space typically provides excellent foam control. 1,000 L and 2,000 L systems can benefit from the use of a condenser system. It has been shown to increase system reliability at high flow rates (beyond 50 slpm) and should warrant strong consideration when performing batch runs beyond 10 days. Results will vary; however, it is strongly recommended that end users select a vent filter configuration providing reserve capacity where possible. For example, dual vent configurations can be used independently with the second filter serving as a redundant backup (providing a quick reserve in case issues arise in process).

Graph 3.3. Off-gassing management guidelines.



Condenser system setup

1. Remove the reservoir cap of the chiller and add the appropriate type and volume of fluid as per the chiller user's guide.
2. Verify that the peristaltic pump and chiller power cords are connected to a power source.
3. If you are using a condenser system with a cart assembly, plug in the system.
4. Turn on the power to the chiller. This will allow the chiller to prime.
5. If you are using a temperature control unit (TCU), ensure that the TCU coolant is filled to the maximum level.

CAUTION: Low TCU coolant levels can increase the temperature of the plates, and cause excessive pressure and/or residue buildup in the condenser bag. Please note that the chiller plates may run warmer than the TCU setpoint.

6. Purge the chill plate by loosening the bleed plug on top of the plate. This is accessed using a hex wrench passing through the top tensioning plate of the chill plate assembly. Loosen the plug only enough to allow trapped air to escape, then re-tighten.
7. The settings for the chiller and peristaltic pump are preset at the factory. These settings allow for the system to resume setpoint if the power is temporarily disrupted. Verify that the chiller and pump setpoints are at the recommended levels (5°C and 12 rpm).
8. If you are using a condenser system with a cart assembly, verify that the peristaltic pump is in place on the cart beneath the chill plate. Side-mounted condenser systems have an attached tray for the peristaltic pump.

Condenser system loading

Two operators are required to safely set up the exhaust system. Setup time is typically 2–3 minutes.

Note: The figures in this section show a condenser system with a cart assembly. Side-mounted condenser systems have the same chiller plate and use the same loading instructions.

1. One operator, located at an elevated position, should remove the condenser BPC carefully from the polybag packaging. Lower the assembly (directed in a vents-first orientation) to the second operator located at ground level, standing to the rear of the S.U.B. For systems with a cart assembly, the second operator should stand between the condenser cart and the S.U.B.
2. The operator at the upper position should move to ground level, open both doors on the chiller plate, and load the condenser BPC from the front, keeping the BPC in a saddle bag shape. Allow the vents to hang freely (Figure 3.78).



Figure 3.78. Opening the chiller plate doors.

3. Route the gas inlet lines around and behind the vent holders, and inspect both lines to ensure they are connected to the S.U.B. and are not twisted or kinked, adjusting them as needed (Figure 3.79).



Figure 3.79. Routing gas inlet lines.

4. The second operator should hold the vent filters and place them into the vent filter holders above the chill plate (Figure 3.80).



Figure 3.80. Placing vent filters.

5. The first operator should use the Velcro™ straps to secure the filters in position (Figure 3.81).



Figure 3.81. Securing vent filters.

6. Use the grasping tabs to position the container using the two lower button pins on each side of the chiller plate (Figure 3.82).



Figure 3.82. Positioning container.

7. Close the clear side doors while carefully manipulating first the gas inlet line and then the gas outlet line (Figure 3.83) to clear the doors as each is closed and latched (Figure 3.84).



Figure 3.83. Moving gas lines.



Figure 3.84. Latching door.

8. As the doors are closed and latched, the second operator should route the gas inlet lines into the clips behind the vents (Figure 3.85).



Figure 3.85. Clipping gas lines into place.

- The first operator should load the peristaltic tubing into the pump (located on the cart for condenser systems with a cart assembly, or on the tray for side-mounted condenser systems), verifying that there is sufficient slack at each end of the pump tubing. Then align the tubing in the pump channel and close the pump ramp (Figure 3.86).

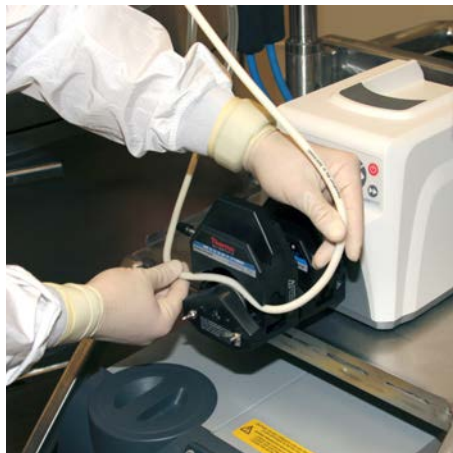


Figure 3.86. Loading pump tubing.

- Start the pump by pushing the red button (Figure 3.87). Verify that both the pump and chiller are enabled and running at the proper settings. We recommend setting the pump at 12–30 rpm and the chiller at 5°C. The specified pumping system is qualified to run continuously (wet or dry) beyond 21 days.

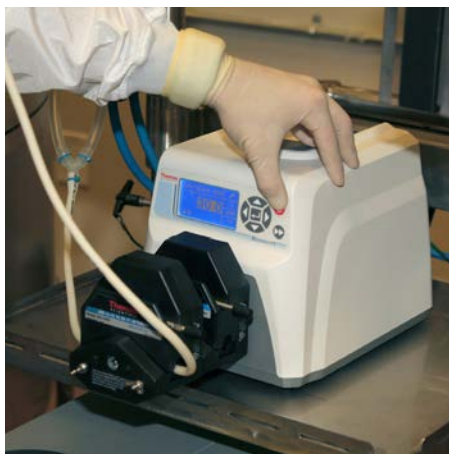


Figure 3.87. Starting the pump.

11. After setup, verify the following:

- ✓ The elbow fittings on the inlet and outlet of the condenser saddle bag are straight and level.
- ✓ The gas inlet line and the condensate line are not twisted, pinched, or obstructed.
- ✓ There are no low spots in the gas inlet line. Adjust the lines to avoid condensation pooling.
- ✓ The pump union is loose on both ends of the pump and running smoothly in the peristaltic rollers.

Contact technical support for specific condenser system performance questions.

3.4.3. Drive shaft insertion for 2,000 L systems

The new drive shafts for 2,000 L S.U.B.s are slightly longer and have black drive shaft heads. Thermo Fisher Scientific has redesigned the impeller in all standard 2,000 L S.U.B. BPCs to improve impeller engagement with this new drive shaft design. 2,000 L 5.1 BPCs are shipped with a hanging tag on the bearing port showing the required drive shaft length (Figure 3.88).

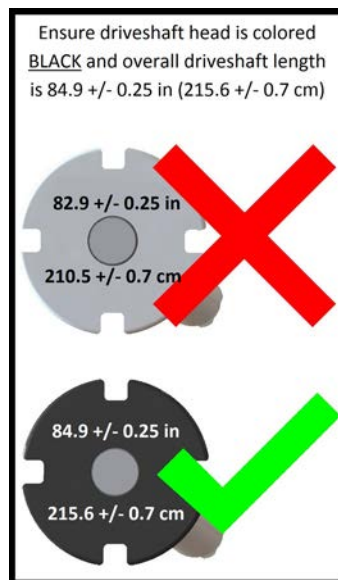


Figure 3.88. Close-up view of 2,000 L 5.1 BPC hanging tag.

The drive shaft is constructed by assembling two quick-connect segments. Operators should be elevated (i.e. ladder) to assemble and insert the drive shaft.

CAUTION: Review ceiling height requirements for the drive shaft in the specifications in Chapter 4.

Figure 3.89 illustrates the components of the motor and mixing assembly. The parts labeled on the figure will be referenced throughout the drive shaft insertion process.

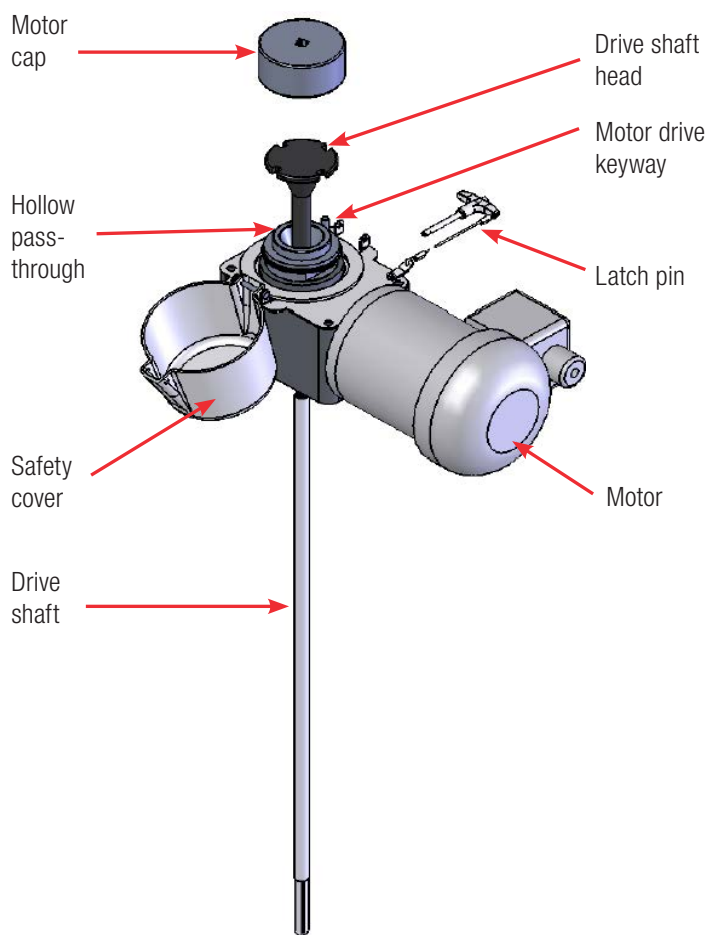


Figure 3.89. Motor and mixing assembly.

Use the following steps to insert the drive shaft.

1. The BPC must be filled with air to greater than approximately 50% volume to allow for unrestricted loading of the angled drive shaft.
Note: After inflation, the impeller tubing should be hanging straight down inside the BPC, with the impeller near the bottom.
2. Verify that the proper drive shaft segments and tools are available.
3. Prepare the hollow pass-through by first removing the latch pin on the safety cover (Figure 3.90), opening the safety cover (Figure 3.91), and removing the threaded cap by turning it counterclockwise. Use the wrench and spanner provided if required.



Figure 3.90. Removing latch pin.



Figure 3.91. Opening safety cover.

- Verify that the two segments of the drive shaft have matching serial numbers, and are located in the drive shaft holders on the side of the outer support container.

Important notes: Always verify that the drive shaft segments have matching serial numbers prior to assembly and use. No lubrication is required with the quick-connect assembly design.

- First, insert the lower segment through the hollow pass-through of the mixer drive (Figure 3.92). Once inserted, slide the latch pin from the mixing assembly into the shaft to prevent it from falling into the impeller sleeve (tube) (Figure 3.93).



Figure 3.92. Insertion of the lower section of the drive shaft.



Figure 3.93. Using the latch pin.

- To connect the upper and lower sections together, depress the button on the female side (Figure 3.94) and slide the sleeve back. This will expose a red ring underneath the sleeve (Figure 3.95). This is a visual indicator that the sleeve is not in a locked position.



Figure 3.94. Button used for connection.



Figure 3.95. Sliding sleeve exposing red "not locked" indicator.

- Place the female side of the quick-connect over the male end (Figure 3.96). The connection is fully seated when the red indicator ring (Figure 3.97) on the male end is no longer exposed.



Figure 3.96. Quick connection.



Figure 3.97. Red indicator ring exposed.

- Slide the sleeve toward the connection, allowing the push button to lock into position. This will engage the locking mechanism and also cover the red indicator ring (Figure 3.98). **Note:** When fully connected, no red coloring should be visible.



Figure 3.98. Sliding the sleeve into place.

- Once the sections are secure, remove the latch pin and return the wrenches to the tool holder.
- Using two hands, carefully guide the completed drive shaft into the BPC using a slight back-and-forth twisting motion or a counterclockwise rotation (Figure 3.99). **Do not push the drive shaft straight in.**

- When 50.8–76.2 mm (2–3 in.) of shaft remains, twist slightly to engage the impeller.
- When 25.4–50.8 mm (1–2 in.) of shaft remains, twist slightly to engage the bearing assembly (Figure 3.100).
- When 6.4 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 3.99. Insertion of the drive shaft. Figure 3.100. Engaging the bearing port.

11. Ensure that the head is fully seated before directly coupling the drive shaft to the motor. Any spring-back indicates that the drive shaft is not properly seated in the impeller. Figure 3.101 illustrates a drive shaft that is completely inserted into the impeller.

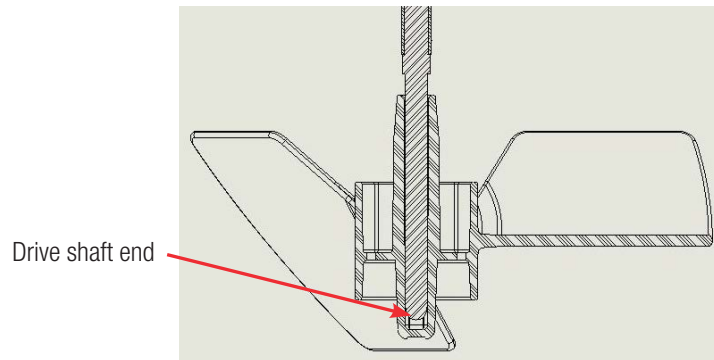


Figure 3.101. Drive shaft fully inserted into the impeller.

Note: The cap should be easy to install when the drive shaft head is fully engaged in the hollow pass-through. Otherwise, repeat steps 1 through 13 before installing the cap.

12. Place the threaded cap back on the hollow pass-through. Secure the cap by placing a spanner wrench on the hollow pass-through and tightening using the supplied torque wrench (Figure 3.102).



Figure 3.102. Tightening cap.

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.).

13. Verify that the wrenches have been removed from the system and returned to the storage holders.
14. Close the safety access cover and insert the latch pin.

3.4.4. Final installation steps for 2,000 L systems

1. Verify the proper position of the exhaust filters. The exhaust flow path must be unobstructed. Connect the gas supply lines. Verify the intended flow paths for overlay, cross flow, and drilled hole spargers.
2. Verify that the overlay and direct sparger lines are correctly positioned and free of kinks. Verify that the rear access door is closed with proper latch tension.
3. Remove the polybag from the drain line set and verify that the redundant line clamps are in position. Use a cable tie around the clamp to ensure the clamp cannot be accidentally opened.

- Align the aseptic ports through the front access window (Figure 3.103).



Figure 3.103. Aseptic port alignment.

- Secure the access doors with the latches. Proper tension is obtained by adjusting the threaded latch pin. Tension of the latch is adjusted by varying the position of the pin on the threaded shank. The proper latch tension can be obtained by a combination of feel and visual inspection. When closing the latch, the handle should begin to provide resistance to closing when the leading edge of the safety pin pass-through of the latch handle aligns with the outside edge of the latch base (Figure 3.104).

Note: When the latch is under-tensioned, the safety pin pass-through of the latch handle will be covered within the latch base and the handle will close very easily. If the latch is over-tensioned, the handle will be excessively difficult to close.



Figure 3.104. Latch access door.

6. For maximum security, insert pins (not included) into the respective latches.
7. Turn off the air supply to the overlay line.
8. Position clamps as close as possible to the BPC and close them on all tube ports (Figure 3.105).



Figure 3.105. Clamp installation.

9. Place clamps on subsurface lines as close to the port as possible. This will eliminate media from filling these lines prior to use.
10. Remove the plastic insert located in the thermowell, if present.
11. Insert the RTD or selected temperature sensor into the thermowell (Figure 3.106).



Figure 3.106. Insertion of the RTD into the thermowell.

- Place a small amount (0.5 mL) of glycerol (Sigma-Aldrich™ G6279) in the thermowell to aid in heat transfer.
 - The sensor should be inserted until the base of the RTD meets the mouth of the thermowell.
 - If provided, secure by twisting the luer lock collar. The thermowell will stretch slightly when the RTD is seated.
12. Connect the batch-to-tank grounding cable to the stainless steel connector of the sample line (Figure 3.107).



Figure 3.107. Grounding cable connected

Note: Verify that all of the port clamps are closed and located as close as possible to the body of the BPC.

13. IMPORTANT: During media fill, verify the position of all critical ports (drain, spargers, line sets, and probes) before the container is filled with more than 50 liters of liquid. This will still allow time for adjustments, if required, after the fill is initiated.

14. Typically, two fill lines (12.7 mm [0.5 in.] x 19.1 mm [0.75 in.]) and peristaltic pumps are recommended to fill the 2,000 L S.U.B. in a timely manner.

3.5. Probe preparation and insertion

3.5.1. Preparation and sterilization

1. Select the appropriate probe (see section 1.3.1). Verify the presence of a Teflon™ support ring and O-ring on the probe and visually inspect the probe for damage.
2. Perform any required probe maintenance and calibrate the pH probe (see section 3.5.4 for probe calibration information).
3. Insert the probe into the probe assembly through the threaded adapter.
4. Verify that the probe tip is not touching (more than 6.35 mm [0.25 in.] gap) the membrane of the aseptic connector before threading into the probe adapter.
5. Hand-tighten the adapter and verify that the probe tip is not touching the membrane.
6. Place the probe assembly with probe into the autoclave tray for probe kits (Figure 3.108).

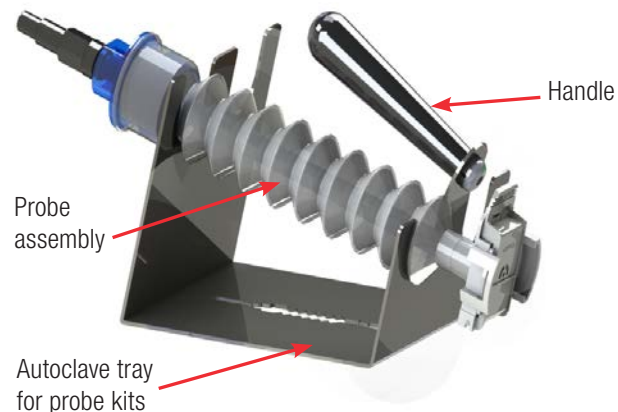


Figure 3.108. Probe assembly and autoclave tray.

7. Autoclave the probe assembly using a validated sterilization cycle (approximately 30 minutes at 122°C). A 30-minute sterilization cycle is generally sufficient. Options of wet or dry cycle parameters can be used. Slow exhaust cycles are preferred, as this minimizes stress on the probes during the temperature and pressure changes of autoclaving.
8. Allow sufficient time for the probe assembly to cool completely before connecting to the BPC for probe insertion.
9. When stored properly, autoclaved probe assemblies can be stored dry for short periods of time (less than 24 hours) without loss of sensor longevity, performance, or sterility.

3.5.2. Making CPC AseptiQuik connections

CPC AseptiQuik G genderless connector components

Figures 3.109 and 3.110 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 following section.



Figure 3.109. CPC AseptiQuik G connector (closed).



Figure 3.110. 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 3.111 and 3.112).



Figure 3.111. Pulling the tear strip.



Figure 3.112. Removing plastic covering from connector.

2. Unsnap and flip open the protective cover pull tabs on both connectors (Figures 3.113 and 3.114).



Figure 3.113. Opening protective cover pull tab on port.



Figure 3.114. Opening protective cover pull tab on lineset.

3. Align the two connectors and push them together.
4. Squeeze each side of the connectors until you hear a click (Figure 3.115).



Figure 3.115. Squeezing connectors together.

5. Grab the joined pull tabs and pull upward to remove the paper membranes from the connectors (Figure 3.116). The pull tabs will also be removed.



Figure 3.116. Pulling tabs to remove paper membranes.

3.5.3. Probe insertion

Before beginning probe insertion, please become familiar with the aseptic connector procedure outlined in section 3.5.2.

6. Attach probe clips onto the outer support container above the probe assembly (Figure 3.117). Plastic probe clips slide on with firm pressure.



Figure 3.117. Attaching plastic probe clip.

7. Install the pre-sterilized sensor and probe kit using the aseptic connection methods described in section 3.5.2. The aseptic connection is completed prior to the bellows being collapsed.
8. Insert the probe by collapsing the bellows (Figures 3.118 and 3.119). **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 3.118. Probe insertion.



Figure 3.119. Collapsed bellows.

9. Position the probe clip in the desired horizontal location. Lift the probe and set it into the probe clip (Figure 3.120).



Figure 3.120. Positioning probe clip.

10. Rest the probe in the bellows hook. Release the probe assembly and verify that the probe remains at the proper insertion depth and angle when the bellows expand to rest freely in the probe clip.

3.5.4. Probe calibration

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

- If you are using a liquid batch-to-tank grounding cable with the stainless steel connector of the sample line, the sample line should be purged of air prior to probe calibration.
- pH probes must be calibrated prior to steam sterilization; the calibration of the probe can be standardized by comparison of an off-line sample once the pH probe has been connected to the S.U.B.
- Dissolved oxygen probes are generally calibrated after steam sterilization. They can be calibrated once the probe is connected to the S.U.B. and is given time to polarize (six to eight hours of continuous connection to the power supply provided by a controller or polarization module).

3.6. Cell culture operating instructions

3.6.1. Operating conditions for cell culture applications

Optimal operating parameters for cell culture vary greatly between cell lines and media formulations. Table 3.7 in section 3.6.8 is provided as a reference for establishing safe 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.

In many cell culture operations, the limits listed in Table 3.7 are excessive and should be further reduced when possible. When reducing gas flow rate limits, the following trade-offs should be expected.

- Reducing drilled hole sparger maximum operating limits will reduce system foaming but increase reliance on O₂. A suggested gas operating control strategy is to run the drilled hole sparger on air initially, and after total flow rate limits are reached, substitute oxygen as shown in Graph 3.5.
- Reducing overlay maximum operating limits will reduce the exhaust load (increasing filter lifespan) but will sacrifice sparger performance if reduced far enough to allow CO₂ buildup in the headspace.

If cell culture density is not increasing at expected rates, this may be due to CO₂ buildup in the headspace. Increasing air flow in the headspace may resolve this problem.

3.6.2. Checkpoints prior to media fill

Verify the following before proceeding to liquid fill.

- ✓ The BPC has been loaded into the hardware by following the instructions provided in sections 3.2, 3.3, or 3.4.
- ✓ All aseptic connector port heavy-duty clamps are closed and located as close as possible to the BPC.
- ✓ The exhaust filter is upright and secured using the holder.
- ✓ The clamp on the drain tube is closed and located as close as possible to the BPC.
- ✓ The temperature RTD is completely seated in the thermowell and secured.
- ✓ The air-filled BPC is properly oriented in the outer support container and the BPC bottom tabs are secured.
- ✓ The gas line sets are connected to the drilled hole sparger and either the cross flow sparger (for 5:1 operation) or overlay sparger (for 2:1 operation).
- ✓ All gas filters are placed above the maximum liquid level.
- ✓ The load cell display has been tared.
- ✓ The motor is in the "down" position (1,000 L and 2,000 L systems only)
- ✓ All sensors are inserted and connected to their respective transmitters. Sensors must be properly oriented to ensure that they are below the liquid level after media fill.

3.6.3. Media fill

1. Select the desired line set from the BPC for fluid introduction.
2. Make an aseptic connection (tubing welder, quick-connect, or tri-clamp) and begin liquid fill.
3. After no more than 20 liters have been added, verify the position of the BPC in the outer support container, particularly the sparger and the drain line. Adjust positioning if necessary for proper fit.
4. Pull the top corners of the BPC upward to reduce wrinkles during filling. **Note:** If the BPC wrinkles are not eliminated during liquid fill, excessive film tension below the bearing port will result.
5. Fill to the desired liquid volume (20–100% of the rated volume is recommended).
6. Ensure that all sensors are below the liquid level after the BPC has been filled.

3.6.4. Agitation for units with electrical control panels

1. After the media has reached the desired liquid volume, use the motor controller power switch to start the agitation using the electrical control panel (E-Box) (Figure 3.121).



Figure 3.121. Front view of E-Box for 50–2,000 L S.U.B.s.

2. Using the arrow keys on the motor speed control keypad, adjust the setpoint speed to the desired level. The adjustment of the stirring speed rpm is done using Hz. The display reverts back to displaying rpm after 2–3 seconds of inactivity. Adjust desired agitation rate within the recommended range as described in Table 3.3.
3. Allow the speed to stabilize, then make fine adjustments if necessary.

Table 3.3. Recommended agitation rates. The values given are based on a standard scale-up criteria of power input to working volume (P/V) using an estimated power impeller number of 2.1, not the parameters of the motor. For rated maximum and minimum operating speeds for the motor, see the hardware specifications in Chapter 4 of this user's guide. For information on calculating agitation rates using power input to volume ratios, see section 3.6.5—Agitation Rate Calculations.

Power ratio	10 Watts per meters ³ (rates in rpm)			Nominal agitation 20 Watts per meters ³ (rates in rpm)			40 Watts per meters ³ (rates in rpm)			Impeller diameter (cm)
	20% working volume	50% working volume	100% working volume	20% working volume	50% working volume	100% working volume	20% working volume	50% working volume	100% working volume	
50 L	85	115	145	107	145	183	N/A	183	230*	11.1
100 L	68	92	116	85	116	146	N/A	146	184	14.6
250 L	54	74	93	69	93	117	N/A	117	148	20.0
500 L	47	64	80	59	80	101	N/A	101	127	25.1
1,000 L	39	53	67	50	68	86	N/A	86	109	32.1
2,000 L	35	47	59	44	60	75	N/A	**	**	39.8

* This value is outside the recommended operating motor range of 30–200 rpm (VFD settings). See Table 4.1 in Chapter 4.

** Consultation with Thermo Scientific engineers is required.



WARNING: Agitation must be stopped when the liquid level falls below 20% of the rated working volume, otherwise damage to the hardware or BPC may result. Do not exceed a 20 W/m³ power ratio when operating between 20% and 50% working volume. See the Warnings, Safety, and Warranty Information section in the front of this publication, and section 3.6.5 for more information about using safety interlocks and agitation speed governors on the controller.

3.6.5. Agitation rate calculations

Using power input to volume ratios for agitation speed

The power input to volume ratio (P/V) allows for scale-up or scale-down of bioreactor platforms by equating mixing power between differently-sized systems. P/V is the most broadly accepted method for determining a practical scale-up approach for agitation speed in stirred tank reactors used for animal cell culture. This relationship is dependent on the density of the liquid in the system (ρ), the inherent power number of the impeller (N_p), the diameter of the impeller (D_i), the volume of liquid in the vessel (V), the speed of the drive shaft in rpm (n), and the power input to the liquid (P).

$$P/V = \frac{N_p * \left(\frac{n}{60}\right)^3 * \rho * D_i^5}{V}$$

This relationship can be rearranged to solve for mixing speed as a function of the other variables.

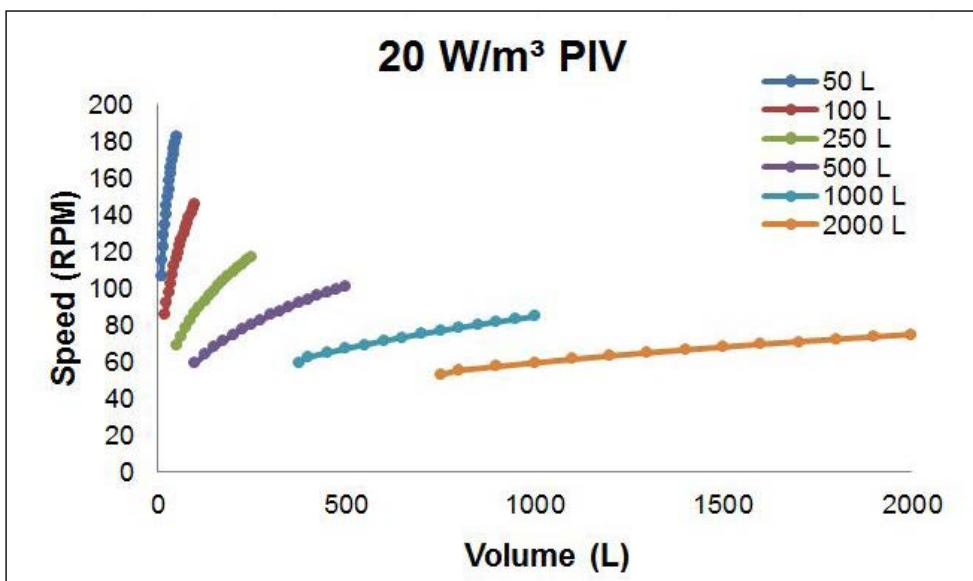
$$n = 60 * \left(\frac{P/V * V}{N_p * \rho * D_i^5}\right)^{\frac{1}{3}}$$

For known values of P/V, impeller power number, density, and impeller diameter, this equation can be simplified by consolidating all other values into a single coefficient (A).

$$n = A * V^{\frac{1}{3}}$$

Values for appropriate agitator drive shaft speed were calculated for different sizes of S.U.B.s using 20–100% of the rated working volumes. These values assume an impeller power number of 2.1, viscosity similar to water, and a constant density of 993 kg/m³.

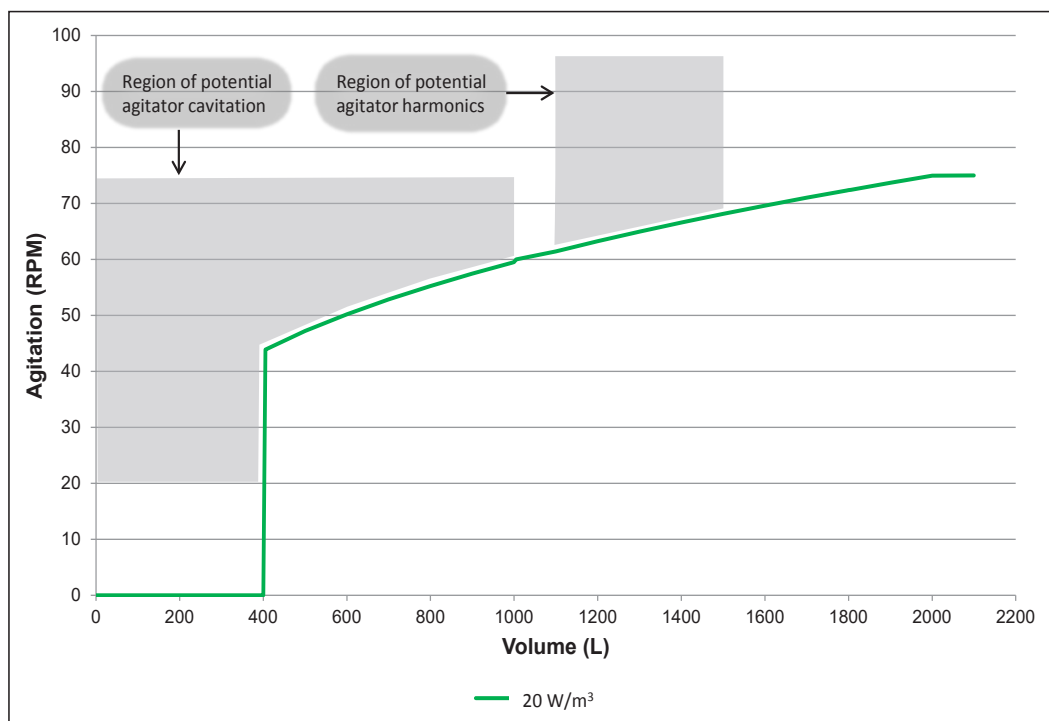
Values of 20 watts/meter³ (W/m³) provide the nominal rating (the suggested default parameter for CHO cultivation), and values of 40 W/m³ provide the maximum recommended parameter that has been qualified for use in the system. Graph 3.4 is provided as a reference, showing the 20 W/m³ P/V curve. While some discrete values are shown, in practice it is acceptable to operate at lower speeds to suit special needs.

Graph 3.4. Nominal agitation values using P/V of 20 W/m³.

Fed batch cultures present unique challenges to the operation of the 2,000 L S.U.B because the fluid height can change dramatically through the duration of a fed batch cell culture run. This drastic change in operating fluid height requires a very long agitator shaft supporting the impeller, requiring it to sustain significant forces of rotating torque and deflection of stress. The 2,000 L S.U.B. was originally qualified to operate reliably when using discrete working volumes of either 1,000 L or 2,000 L with a maximum recommended operating speed of 75 rpm. This represented a worst case P/V of 40 W/m³ (1,000 L) and best case of 20 W/m³ (2,000 L) as the extra volume and column height at 100% working volume offer significant protection against drive shaft instability.

An in-depth study of the 2,000 L S.U.B. has shown that harmonics can begin to propagate fatigue into the drive shaft when the system is operated between 1,100 L and 1,500 L when the agitator P/V is above 20 W/m³. In order to maximize shaft life and reliability, it is important to scale P/V with this constraint in mind. See Graph 3.5 for values of potential cavitation and harmonics. It is recommended to operate your S.U.B. at agitation values below the green curve.

Graph 3.5. Regions of potential agitator harmonics and cavitation for various liquid working volumes of the 2,000 L S.U.B. The green line represents a P/V of 20 W/m³. It is recommended to operate 2,000 L S.U.B.s below this curve.



P/V agitation values for all S.U.B. sizes

Equation coefficient values for every size of S.U.B. for P/V values of 20 and 40 watts/meter³ (W/m³) are provided in Table 3.4 below.

Agitation speeds for P/V values of 20 and 40 W/m³ are provided in Tables 3.5 and 3.6.

Table 3.4. Equation coefficient values (A) for different S.U.B.s.

$n = A \times V^{1/3}$ (for values of n in rpm)						
	50 L S.U.B.	100 L S.U.B.	250 L S.U.B.	500 L S.U.B.	1,000 L S.U.B.	2,000 L S.U.B.
P/V						
20 W/m ³	49.650	31.491	18.634	12.764	8.471	5.950*
40 W/m ³	62.554	39.676	23.477	16.081	10.673	7.031**

* Coefficient value is used to determine operating speeds for drive shafts implemented for a 180-day working duration at 20 W/m³.

** Consult Thermo Scientific engineers for the drive shaft working duration at > 20 W/m³.

Table 3.5. Agitation rates (in rpm) for S.U.B.s at a P/V of 20 W/m³.

	50 L S.U.B.	100 L S.U.B.	250 L S.U.B.	500 L S.U.B.	1,000 L S.U.B.	2,000 L S.U.B.*
Fill %						
100	183	146	117	101	86	75
95	180	144	115	100	83	74
90	177	141	113	98	82	72
85	173	138	111	96	80	71
80	170	136	109	94	79	70
75	166	133	107	92	77	68
70	162	130	104	90	75	67
65	158	127	102	88	73	65
60	154	123	99	85	71	63
55	150	120	96	83	69	61
50	145	116	93	80	68	60
45	140	112	90	78	65	57
40	135	108	86	75	62	55
35	129	103	83	71	60	53
30	122	98	79	68	57	50
25	115	92	74	64	53	47
20**	107	85	69	59	50	44
<p>* Using these rpm values requires replacement of the drive shaft after 180 days of use.</p> <p>** These rpm values assume the system is operating at no less than 20% volume. In order to ensure proper volume measurements, end users are responsible for ensuring proper load cell calibration prior to system use.</p>						

Table 3.6. Agitation rates (in rpm) for S.U.B.s at a P/V of 40 W/m³.

	50 L S.U.B.	100 L S.U.B.	250 L S.U.B.	500 L S.U.B.	1,000 L S.U.B.	2,000 L S.U.B.
Fill %						
100	230	184	148	127	109	*
95	227	181	145	125	105	*
90	222	178	143	123	103	*
85	218	174	140	121	101	*
80	214	171	137	118	99	*
75	209	167	134	116	97	*
70	205	164	131	113	95	*
65	200	160	128	111	92	*
60	194	155	125	108	90	*
55	189	151	121	105	87	*
50	183	146	117	101	86	*
45	177	141	113	98	82	*
40	170	136	109	94	79	*
35	162	130	104	90	75	*
30	154	123	99	85	71	*
25	145	116	93	80	67	*
20**	135	107	86	75	64	*

* Consultation with Thermo Scientific engineers is required when operating 2,000 L S.U.B.s at a P/V of > 20 W/m³.

** These rpm values assume the system is operating at no less than 20% volume. In order to ensure proper volume measurements, end users are responsible for ensuring proper load cell calibration prior to system use.

Please note: The impeller power number assumption of $N_p=2.1$ is only an approximation, based on an academic exercise. Recommended best practice for determination and comparison of N_p between bioreactors should be carried out by the end user and should be based on conditions matching the specific application. End users should also anticipate and accept some variability that may be inherent in the analysis technique or modeling method chosen. If a different or alternative N_p value is determined by the end user, the safety interlocks must be based solely on the maximum prescribed rpm for a working volume as found in the reference tables in this publication. **Never rely strictly on an estimated magnitude of P/V when setting the agitator speed interlock levels.**

3.6.6. Drive shaft rotation

Verify that the drive shaft is rotating counterclockwise when viewed from the top looking down. The S.U.B. is designed to mix in this direction only.

3.6.7. Temperature control

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

1. Connect to an external TCU using the large couplings located on the vessel jacket. Ensure the inlet/outlet ports are connected properly; improper installation may result in poor heating/cooling performance.
2. Open the valves after connecting the TCU (Figure 3.122).



Figure 3.122. Opening valves.

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

3.6.8. Sparging strategy

Sparging strategy and gas supply setup

Standard 5.1 BPCs are supplied with drilled hole, overlay, and cross flow spargers. Figure 3.123 illustrates the location of each sparger on a standard 500 L BPC. The cross flow sparger is used to reduce carbon dioxide buildup in the headspace near the liquid surface when the liquid volume is at 20%.

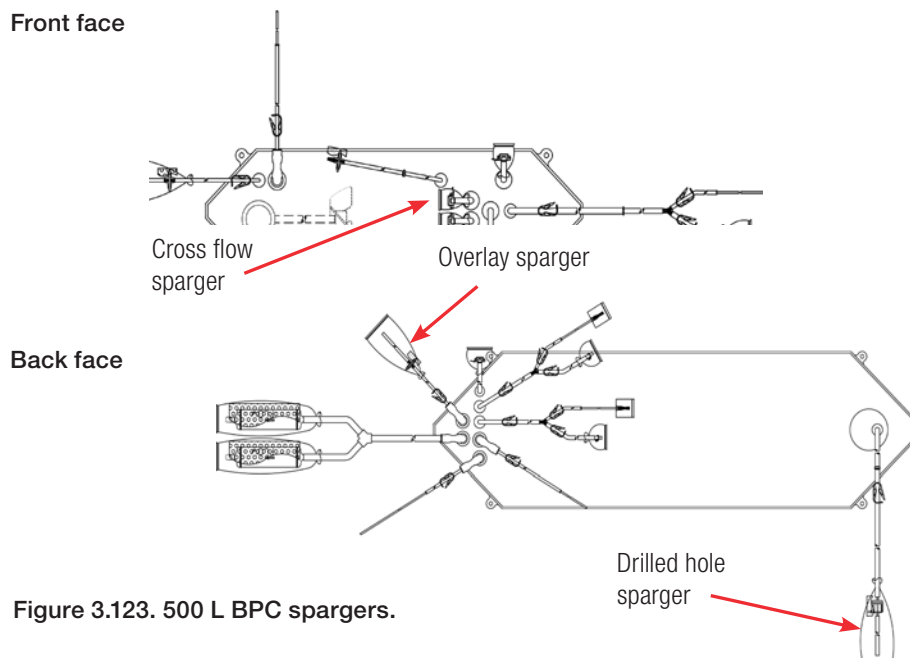
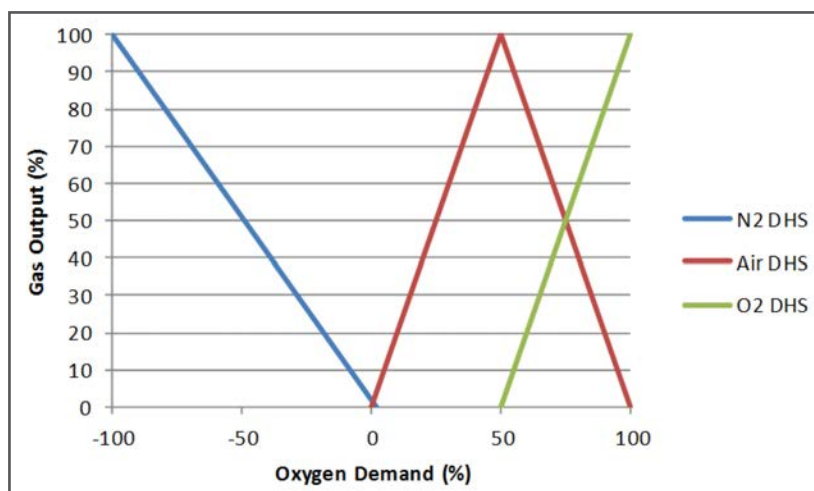


Figure 3.123. 500 L BPC spargers.

Graph 3.6 depicts a dissolved oxygen (DO) management strategy. Refer to Table 3.7 in the following section for gas flow rate recommended maximum values. In developing a gassing strategy for a S.U.B. with a drilled hole sparger configuration, it is optional to have a cross over from nitrogen to air when progressing from negative to positive DO control. Graph 3.6 depicts a minor crossover.

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

Graph 3.6. Drilled hole sparger DO control strategy for 5.1 S.U.B. systems.



Gas flow rates

Standard 5.1 BPCs are supplied with drilled hole, overlay, and cross flow spargers. If foaming or exhaust filter load/lifespan is of primary concern, priority should be placed on tuning the system to operate primarily by adding oxygen through the drilled hole sparger. If carbon dioxide stripping is of primary concern, priority should be placed on running the drilled hole sparger at flow rates sufficient to reduce or eliminate the need for base addition.

Table 3.7 contains a listing of operating parameters for all sizes of S.U.B.s. This data may be used in specifying maximum gas flow rates for mass flow controllers or rotameters when using drilled hole spargers. In optimal conditions, without condensation or fouling, the exhaust filters have a flow capacity of at least 20 and 90 slpm (standard liters per minute) at 0.006 bar (0.1 psi) for the small and large standard equipped filter types. The total flow rate of gas into the system must be less than the sum flow rate capacity of active exhaust filters.

The values listed take into account the number and type of exhaust filters that are standard on each size of S.U.B. (one small filter installed in the 50 L and 100 L, one large filter installed in the 250 L and 500 L, and two large filters installed in the 1,000 L and 2,000 L vessels). 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.

Table 3.7. Range of operating parameters.

	50 L			100 L			250 L			500 L			1,000 L			2,000 L		
Temperature (°C)	2.0 - 40.0 ± 0.1																	
	10-50			20-100			50-250			100-500			200-1000			400-2000		
Recommended max. gas flow rates (slpm)	DHS	Cross flow	Overlay	DHS	Cross flow	Overlay	DHS	Cross flow	Overlay	DHS	Cross flow	Overlay	DHS	Cross flow	Overlay	DHS	Cross flow	Overlay
Air	5	5	5	10	9	9	25	13	13	50	25	25	100	40	40	200	60	60
	5	-	-	10	-	-	25	-	-	50	-	-	100	-	-	200	-	-
CO ₂	1	-	-	2	-	-	2	-	-	2	-	-	5	-	-	5	-	-
	1	-	-	2	-	-	5	-	-	5	-	-	10	-	-	10	-	-
Total	5	5	5	10	9	9	25	13	13	50	25	25	100	40	40	200	60	60
	20			20			90			90			180			360		

3.6.9. pH probe calibration

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.

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

3.6.10. DO probe calibration

After polarizing for six to eight hours, the DO probe can be calibrated in the S.U.B. using standard protocols. Turn on full air sparging. Do not exceed the maximum gassing rates listed in Table 3.7 in section 3.6.8. Sparge until the DO stabilizes. Use the stabilized value as the 100% DO setpoint for the controller. Set the zero percent DO setpoint by sparging with nitrogen, or by temporarily unplugging the DO probe.

3.6.11. Checkpoints prior to inoculation

Before inoculation, verify that:

- ✓ After the S.U.B. is filled with media to 20% or more volume, BPC tabs have been disconnected from the S.U.B. hardware.
- ✓ The pH probe is calibrated, autoclaved, and connected via an aseptic connector port. Perform 1-point offset on your controller as necessary.
- ✓ The DO probe is autoclaved, connected via an aseptic connector port, polarized (six to eight hours), and calibrated.
- ✓ The temperature RTD is completely seated in the thermowell and secured.
- ✓ Ensure that all sensors are below the liquid level.
- ✓ Operating parameters (temperature, agitation, pH, and DO) are at the desired setpoints.
- ✓ A method for making aseptic tubing connections is available.
- ✓ Air is connected to the cross flow sparger when operating at 20% volume.

3.6.12. Cell inoculation

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

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

Note: For shear sensitive cultures, cells can be introduced by manipulating the addition port to direct the inoculum down the interior wall of the BPC and into the bulk fluid, reducing the shear on the cells. Custom line sets can be supplied with dip tubes, which shorten the distance between the point of inoculum introduction and the bulk fluid level.

3.6.13. Volume scale up

1. Using a sterile process, connect media to the BPC with the media fill port.
2. Begin pumping media into the BPC at the desired flow rate. Ensure that the vessel temperature does not drop below culture limits.
3. Remove the air line from the cross flow sparger, replace onto the overlay gas port, and clamp the cross flow sparger port as close to the BPC as possible.
4. Increase the volume to the desired level.

3.6.14. 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.
- ✓ The cap is tight on the drive shaft.
- ✓ The temperature sensor/RTD is completely seated and secured.
- ✓ No condensate accumulates in exhaust filter housing.
Accumulated condensate indicates that the use of a filter heater is required.

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

3.6.15. BPC sampling

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

Aseptic sampling

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

1. Remove the dust cover from the SmartSite needle-free valve, which is connected to the end of the sample port (Figure 3.124).



Figure 3.124. Removal of dust cover from SmartSite.

2. Clean the SmartSite with a sanitary wipe.
3. Connect the sanitary luer lock type syringe (Figure 3.125).



Figure 3.125. Connecting the syringe.

4. To purge the sample line, apply a small amount of vacuum pressure by pulling out the syringe plunger slightly.
5. Open the pinch clamp and pull a sample (approximately 20 mL), using care not to allow any back flow.
6. Close the pinch clamp and remove the syringe. This will be a purge sample.
7. Clean the SmartSite with a sanitary wipe.
8. Connect the sanitary luer lock type syringe.
9. Pull the sample by applying a small amount of vacuum pressure using the syringe.
10. Open the pinch clamp and pull the desired sample volume (approximately 10–20 mL), taking care not to allow any back flow.
11. Close the pinch clamp and remove the syringe. This will be a representative sample.
12. Clean the SmartSite with a sanitary wipe and replace the dust cap.

Sampling with a sterile manifold

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

1. Remove the manifold from its protective polybag package.
2. Close all of the clamps on the manifold lines.
3. Use a sterile tubing welder to connect the manifold to the sample line (Figure 3.126).



Figure 3.126. Tubing welder.

4. Inspect the welds and open flow path by pinching the welds.
5. Open two clamps at the inlet and the clamp at the purge container (100 mL container).
6. Purge the sample line by filling the purge container (30–60 mL is recommended).
7. Close the clamp nearest to the purge container.
8. Open the clamp to the sample container (50 mL container) (Figure 3.127).



Figure 3.127. 50mL manifold.

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

3.6.16. Dispense and harvest

1. Connect the bottom drain tubing set to the intended transfer line.
2. Open the clamp positioned at the bottom drain port.
3. Begin to drain, using a peristaltic pump.
4. Stop the impeller motor when volume reaches 20% maximum volume.
5. Remove and store the drive shaft by reversing the steps used during assembly.
6. Disable the temperature control to ensure that the S.U.B. does not overheat.
7. 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 toward the drain).
8. Hold the bottom drain line near the floor while lifting the exhaust filter side of the BPC to facilitate draining the final liter of harvest media.

3.6.17. BPC disposal

After the drive shaft has been removed and the BPC has been drained, the BPC can be removed from the outer support container. Filters can be removed and integrity tested as needed according to the user's standard procedures. All product contact materials related to the S.U.B. can be disposed of in an appropriate waste container or incinerator. **Note:** For 2,000 L systems, do not lower the BPC lift until the used bag has been removed from the tank.

3.6.18. S.U.B. shutdown

1. After the run is complete, verify that the motor agitation is off and turn off the power to the outer support container by switching off the main power disconnect.
2. If the S.U.B. hardware has come in contact with caustic materials during the course of a run, rinse the affected areas with a light water rinse, followed by normal routine cleaning (see section 3.6.19).

3. Loose items such as the drive shaft, tools, and RTD probes should be returned to their storage locations to prevent accidental damage.

3.6.19. Preparation for the next run

Between runs, the S.U.B. hardware (outer support container, probe shelf, drive shaft, mixer drive, etc.) can be wiped down with a sanitary wipe. The outer support container can be cleaned with standard stainless steel cleaner. Store the drive shaft in the storage holder located near the handle of the outer support container.

The S.U.B. hardware system can be cleaned to the extent of standard laboratory cleaning procedures. Care should be taken to ensure electrical connections have been disconnected and electrical enclosures are closed tightly. It is also recommended that excess water is not introduced under the heat shield or over the control panel. A wipe-down with normal disinfectant solutions is sufficient. Avoid using excessive amounts of liquid. The unit must be allowed to fully dry prior to being brought back into operation.

3.7. Verification procedures

3.7.1. Mixing speed verification

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

3.7.2. Temperature controller verification

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

3.7.3. Pressure monitor verification (when present)

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

3.7.4. Load cell verification

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

4

System features and specifications

Chapter contents

- 4.1 Hardware features
- 4.2 Hardware specifications
- 4.3 Electrical control panel features
- 4.4 BPC specifications
- 4.5 Additional system component part numbers

4.1. Hardware features

4.1.1. Design features for 50–250 L systems

Figures 4.1 and 4.2 (below) illustrate the hardware features of 50–250 L S.U.B. systems. Electrical control panel (E-Box) features are illustrated in section 4.3.

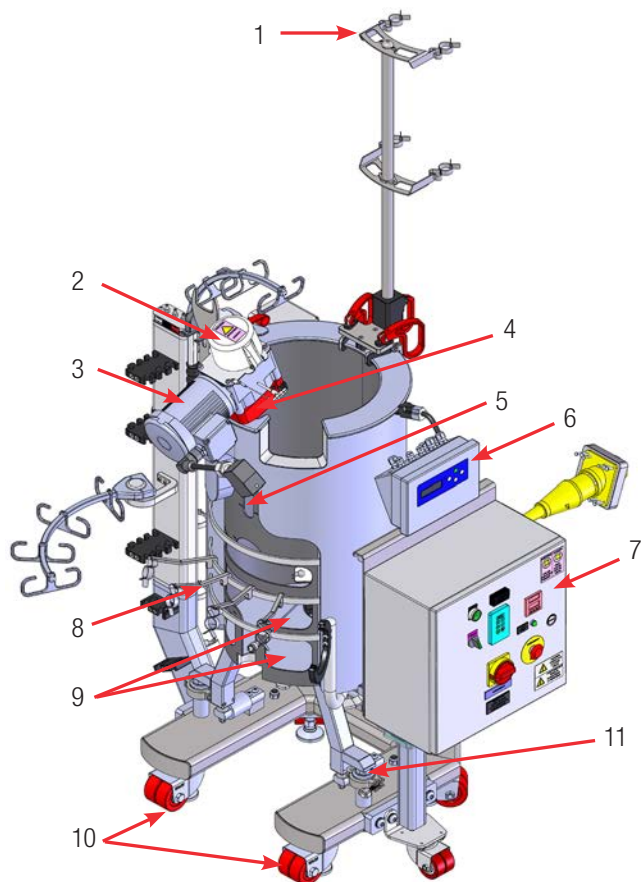


Figure 4.1. Front/side view of 50 L S.U.B.

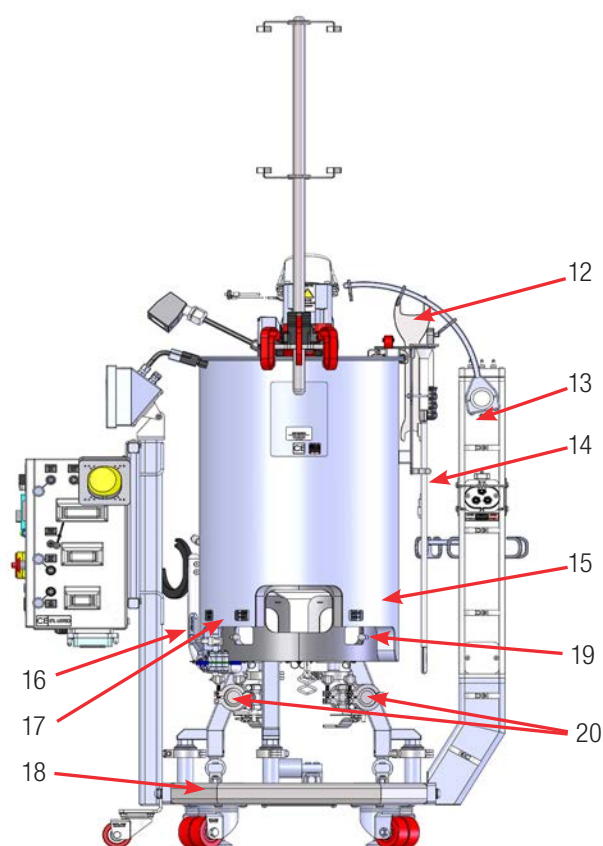


Figure 4.2. Back view of 50 L S.U.B.

1. Exhaust vent filter holder (optional)
2. Mixing assembly with shield
3. Mixer motor
4. Bearing port receiver with clamp
5. Liquid sight windows
6. Load cell display
7. Electrical control panel (E-Box), optional
8. Probe hanger bracket
9. Probe access windows
10. Leveling casters
11. Load cells

12. 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
13. Cable management system
14. Drive shaft, stored
15. Stainless steel (304) outer support container
16. Bleed valve
17. 0.95 cm (3/8 in.) Dimpled jacket (side)
18. Cart assembly
19. Bottom cutouts/pins for BPC attachment/alignment
20. Quick-connect water inlet/outlet ports

4.1.2. Design features for 500 L systems

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

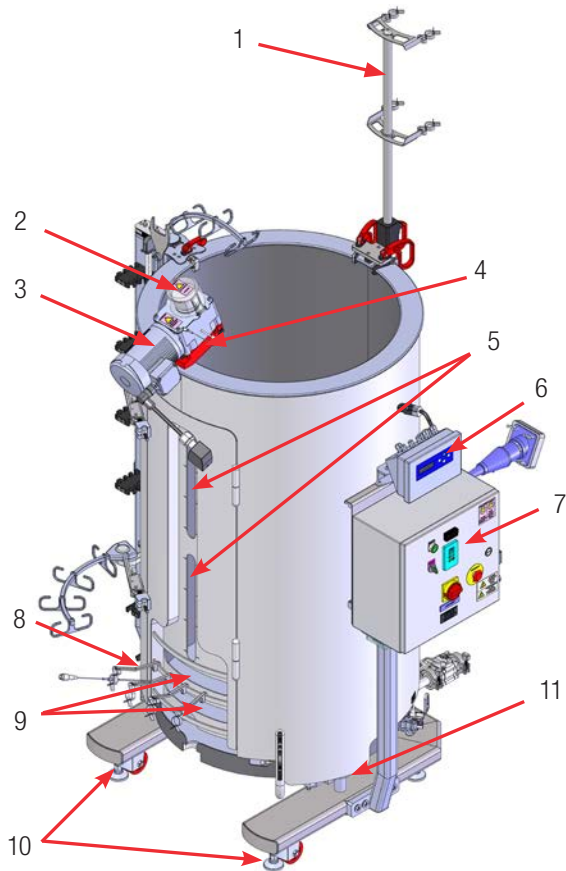


Figure 4.3. Front/side view of 500 L S.U.B.

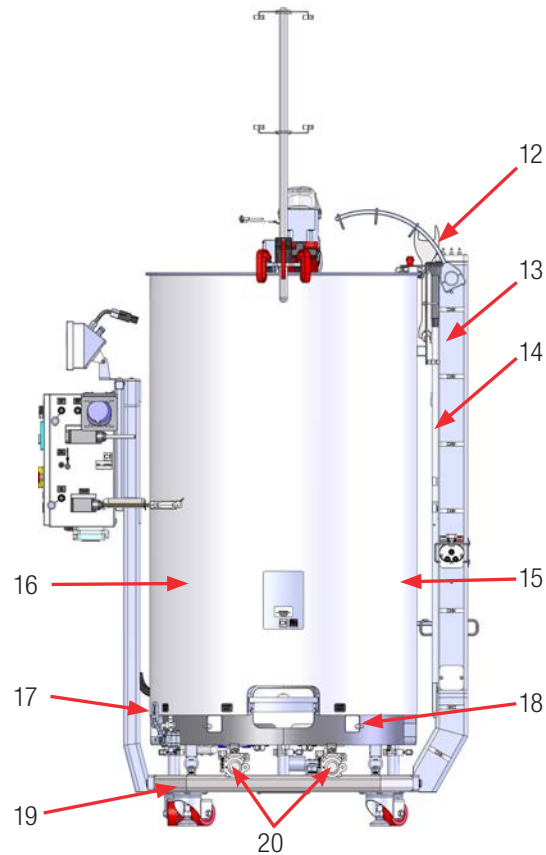


Figure 4.4. Back view of 500 L S.U.B.

1. Exhaust vent filter holder
2. Mixing assembly with shield
3. Mixer motor
4. Bearing port receiver with clamp
5. Liquid sight windows
6. Load cell display
7. Electrical control panel (E-Box), optional
8. Probe hanger bracket
9. Probe access windows
10. Leveling casters
11. Load cells (3)

12. 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
13. Cable management system
14. Drive shaft (2-piece), stored
15. Stainless steel (304) outer support container
16. 0.95 cm (3/8 in.) Dimpled jacket
17. Bleed valve
18. Bottom cutouts/pins for BPC attachment/alignment
19. Cart assembly
20. Quick-connect water inlet/outlet ports

4.1.3 Design features for 1,000 L systems

Figures 4.5 and 4.6 (below) illustrate the features of 1,000 L S.U.B. systems. Electrical control panel (E-Box) features are illustrated in section 4.3.

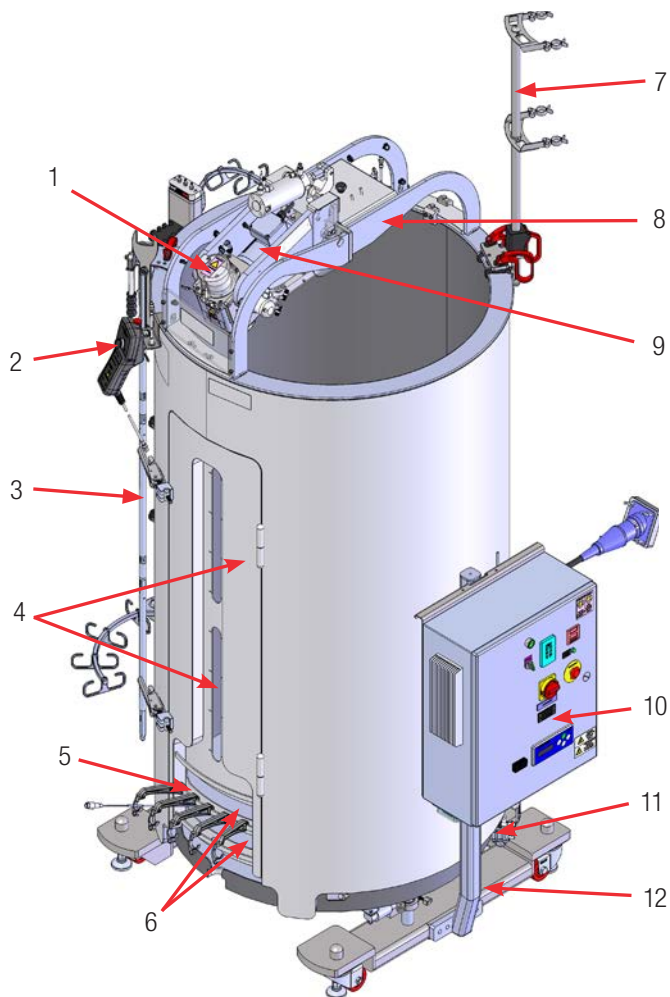


Figure 4.5. Front/side view of 1,000 L S.U.B.

1. Mixing assembly with motor safety shield
2. Handheld controller (on bracket)
3. Drive shaft, stored (3-piece shown)
4. BPC loading door and liquid sight windows
5. Probe hanger bracket (with probe clips)
6. Probe access windows
7. Exhaust vent filter holder
8. Motor lift
9. Mixer motor
10. Electrical control panel (E-Box), optional
11. Load cell (3)
12. Cart assembly

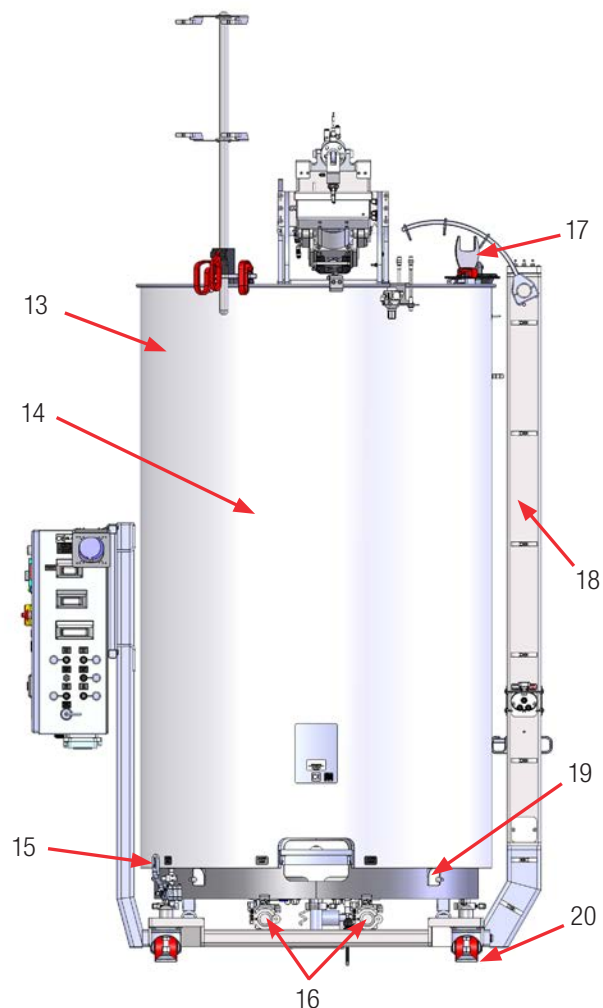


Figure 4.6. Back view of 1,000 L S.U.B.

13. 0.95 cm (3/8 in.) Dimpled jacket
14. Stainless steel (304) outer support container
15. Bleed valve
16. Quick-connect water inlet/outlet ports
17. 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
18. Cable management system (optional)
19. Bottom cutouts/pins for BPC attachment and alignment
20. Leveling casters

4.1.4 Design features for 2,000 L systems

Figures 4.7 and 4.8 (below) illustrate the features of 2,000 L S.U.B. systems. Electrical control panel (E-Box) features are illustrated in section 4.3.

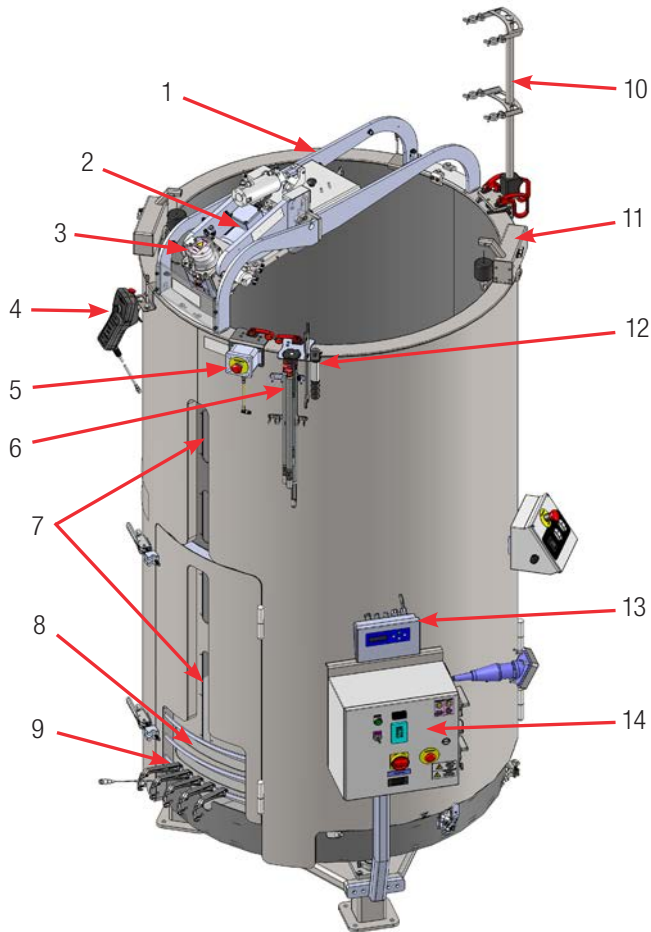


Figure 4.7. Front/side view of 2,000 L S.U.B.

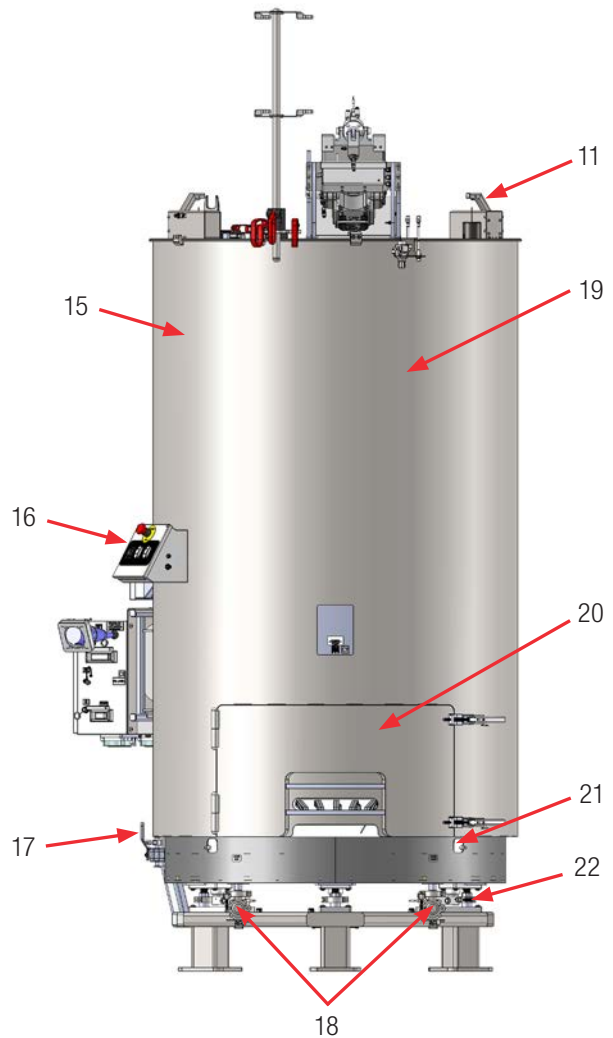


Figure 4.8. Back view of 2,000 L S.U.B.

1. Motor lift
2. Mixer motor
3. Mixing assembly with motor safety shield
4. Handheld controller for motor adjustment (on bracket)
5. Emergency stop button (E-Stop)
6. Drive shaft, stored (4-piece shown)
7. Front access door and liquid sight windows
8. Probe access window
9. Probe hanger bracket (with probe clips)
10. Exhaust vent filter holder
11. BPC lift (2)
12. 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

13. Load cell display
14. Electrical control panel (E-Box), optional
15. 0.95 cm (3/8 in.) Dimpled jacket
16. BPC lift control
17. Bleed valve
18. Quick-connect water inlet/outlet ports
19. Stainless steel (304) outer support container
20. Rear access door
21. Bottom cutouts/pins for BPC attachment and alignment
22. Load cell (3)

4.2. Hardware specifications

The following tables and figures provide specifications for 50 L, 100 L, 250 L, 500 L, 1,000 L, and 2,000 L S.U.B.s. See section 1.2.3 for drive shaft specifications.

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

		AC and DC motors
Bioreactor geometry	Rated liquid working volume	50 L
	Minimum liquid working volume	10 L
	Total reactor volume (liquid & gas)	65.5 L
	BPC chamber diameter	34.9 cm (13.75 in.)
	BPC chamber shoulder height	80 cm (31.5 in.)
	Liquid height at rated working volume	52.1 cm (20.5 in.)
	Fluid geometry at working volume (height/diameter) ratio	1.5:1
	Overall reactor geometry (height/diameter ratio)	1.9:1
Tank baffles	No	
Impeller	Impeller (quantity x blade count)	1 x 3
	Impeller scaling (impeller diameter/tank diameter)	1/3
	Impeller blade pitch (angle)	45°
	Impeller diameter	11.11 cm (4.37 in.)
	Impeller—calculated power number (N)	2.1
Agitation	Agitation speed range	30–200 ± 1.5 rpm or 1% of setpoint, whichever is greater
	Nominal agitation rating—power/volume ratio	20 W/m ³
	Nominal agitation—20% working volume	107 rpm
	Nominal agitation—50% working volume	145 rpm
	Nominal agitation—100% working volume	183 rpm
	Nominal tip speed	103.9 cm/s (204.6 ft./min.)
	Counterclockwise mixing flow direction	Down-pumping
	Agitation shaft resolved angle	16.5°
	Agitation shaft centerline offset	1.9 cm (0.75 in.)
	Overall drive shaft length	85.09 cm (33.5 in.)
	Drive shaft diameter	1.27 cm (0.5 in.)
Drive shaft poly-sheath outside diameter	2.54 cm (1 in.)	
Impeller clearance from tank bottom	4.83 cm (1.9 in.)	

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

		AC motor	DC motor
Motor	Agitation motor drive (type, voltage, phase) AC motor only	Induction, 208 VAC, 3	-
	Agitation motor drive (type, voltage) DC motor only	-	Brushless, 48 VDC
	Motor power rating (AC motor)	186.4 W (0.25 hp)	-
	Motor power rating (DC motor)	-	200 W (0.268 hp)
	Motor torque rating	9.5 Nm (82 in-lb.)	-
	Gear reduction	10:1	-
	Programmable VFD, remote panel interface, power fault auto restart	Standard	-
	Motor communication methods (for external controller)	0-10 V, 4-20 mA, Modbus	-
Temperature control	Jacket area: full/half volume	0.41 m ² (4.4 ft. ²) / 0.19 m ² (2 ft. ²)	
	Jacket volume	2.4 L	
	Jacket flow rate at 3.4 bar (50 psi)	136 L/min.	
	Process connection	1.5 in. Sanitary tri-clamp	
	Nominal heating/cooling load (W)	500 W	
	Approximate liquid heat-up time (5–37°C)—20% volume	1 hr	
	Approximate liquid heat-up time (5–37°C)—100% volume	1.1 hr	
RTD or thermocouple, 3.18 mm (1/8 in.) OD	RTD: Pt-100 (standard)		
Support container	Overall width	94.2 cm (37.1 in.) with E-Box	56.5 cm (22.25 in.)
	Overall length	84.3 cm (33.2 in.) with E-Box	77 cm (30.3 in.)
	Overall height	198.6 cm (78.2 in.)	
	Dry skid weight (mass)	115.7 kg (255 lb.)	
	Wet skid weight—rated working volume (mass)	165.7 kg (365.2 lb.)	
General	Ceiling height required for drive shaft loading	208.53 cm (82.1 in.)	
	Electrical power supply requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A	Dependent on controller
	pH & DO probe—autoclavable type (Applisens, Broadley James, Mettler Toledo)	12 mm diameter x 215–235 mm insertion length x 13.5 PG (pipe) thread	
	Noise level	< 70 dB at 1.5 m	
Recommended operating parameters	Operating temperature range	Ambient to 40 +/- 0.5°C (104 +/- 0.9°F)	
	Motor speed	30–200 rpm	
	Volume range	10–50 L	
	Maximum bag pressure	0.03 bar (0.5 psi)	

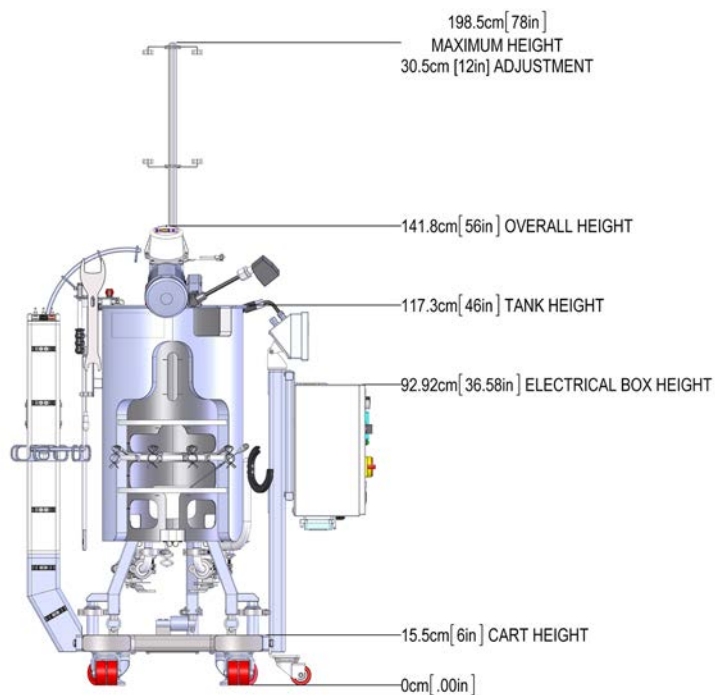


Figure 4.9. Dimensions of 50 L S.U.B. (front view).

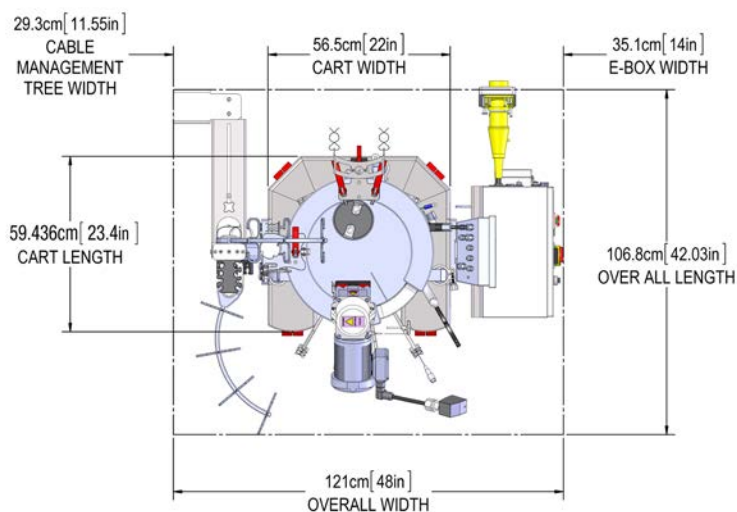


Figure 4.10. Dimensions of 50 L S.U.B. (top view).

Table 4.3. 100 L S.U.B. specifications.

		AC motor	DC motor
Bioreactor geometry	Rated liquid working volume	100 L	
	Minimum liquid working volume	20 L	
	Total reactor volume (liquid & gas)	120 L	
	BPC chamber diameter	43.8 cm (17.25 in.)	
	BPC chamber shoulder height	95.3 cm (37.5 in.)	
	Liquid height at rated working volume	66 cm (26 in.)	
	Fluid geometry at working volume (height/diameter) ratio	1.5:1	
	Overall reactor geometry (height/diameter ratio)	1.9:1	
	Tank baffles	No	
Impeller	Impeller (quantity x blade count)	1 x 3	
	Impeller scaling (impeller diameter/tank diameter)	1/3	
	Impeller blade pitch (angle)	45°	
	Impeller diameter	14.6 cm (5.75 in.)	
	Impeller—calculated power number (N)	2.1	
Agitation	Agitation speed range	30–200 ± 1.5 rpm or 1% of setpoint, whichever is greater	
	Nominal agitation rating—power/volume ratio	20 W/m ³	
	Nominal agitation—20% working volume	85 rpm	
	Nominal agitation—50% working volume	116 rpm	
	Nominal agitation—100% working volume	146 rpm	
	Nominal tip speed	110.7 cm/s (218 ft./min.)	
	Counterclockwise mixing flow direction	Down-pumping	
	Agitation shaft resolved angle	16.5°	
	Agitation shaft centerline offset	2.54 cm (1 in.)	
	Overall drive shaft length	100.58 cm (39.6 in.)	
	Drive shaft diameter	1.27 cm (0.5 in.)	
	Drive shaft poly-sheath outside diameter	2.54 cm (1 in.)	
Impeller clearance from tank bottom	5.08 cm (2 in.)		

Table 4.4. 100 L S.U.B. specifications (continued).

		AC motor	DC motor
Motor	Agitation motor drive (type, voltage, phase) AC motor only	Induction, 208 VAC, 3	-
	Agitation motor drive (type, voltage) DC motor only	-	Brushless, 48 VDC
	Motor power rating (AC motor)	186.4 W (0.25 hp)	-
	Motor power rating (DC motor)	-	200 W (0.268 hp)
	Motor torque rating	9.5 Nm (82 in-lb.)	-
	Gear reduction	10:1	-
	Programmable VFD, remote panel interface, power fault auto restart	Standard	-
	Motor communication methods (for external controller)	0–10 V, 4–20 mA, Modbus	-
Temperature control	Jacket area: full/half volume	0.60 m ² (6.5 ft. ²) / 0.21 m ² (2.3 ft. ²)	
	Jacket volume	4.5 L	
	Jacket flow rate at 3.4 bar (50 psi)	136 L/min.	
	Process connection	1.5 in. Sanitary tri-clamp	
	Nominal heating/cooling load	1,000 W	
	Approximate liquid heat-up time (5–37°C)—20% volume	0.9 hr	
	Approximate liquid heat-up time (5–37°C)—100% volume	1.6 hr	
	RTD or thermocouple, 3.18 mm (1/8 in.) OD	RTD: Pt-100 (standard)	
Support container	Overall width	98.5 cm (38.8 in.) with E-box	56.5 cm (22.25 in.)
	Overall length	91.2 cm (35.9 in.) with E-box	85.8 cm (33.8 in.)
	Overall height	201.5 cm (79.3 in.)	
	Dry skid weight (mass)	160.6 kg (354 lb.)	
	Wet skid weight—rated working volume (mass)	260.6 kg (574.5 lb.)	
General	Ceiling height required for drive shaft loading	232.66 cm (91.6 in.)	
	Electrical power supply requirement (voltage, phase, amp)	120/240 VAC, Single, 20/10 A	Dependent on controller
	pH & DO probe—autoclavable type (Applisens, Broadley James, Mettler Toledo)	12 mm diameter x 215–235 mm insertion length x 13.5 PG (pipe) thread	
	Noise level	< 70 dB at 1.5 m	
Recommended operating parameters	Operating temperature range	Ambient to 40 +/- 0.5°C (104 +/- 0.9°F)	
	Motor speed	30–200 rpm	
	Volume range	20–100 L	
	Maximum bag pressure	0.03 bar (0.5 psi)	

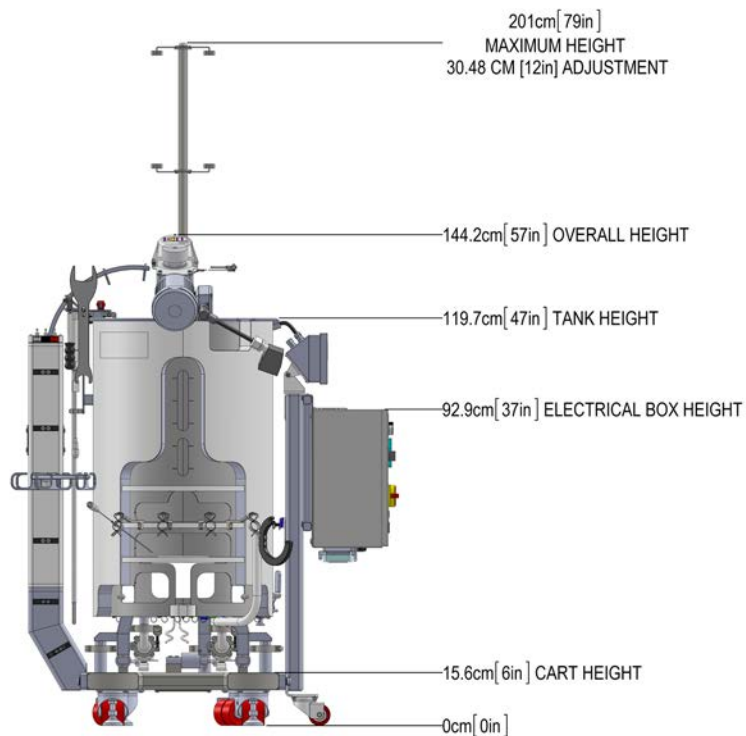


Figure 4.11. Dimensions of 100 L S.U.B. (front view).

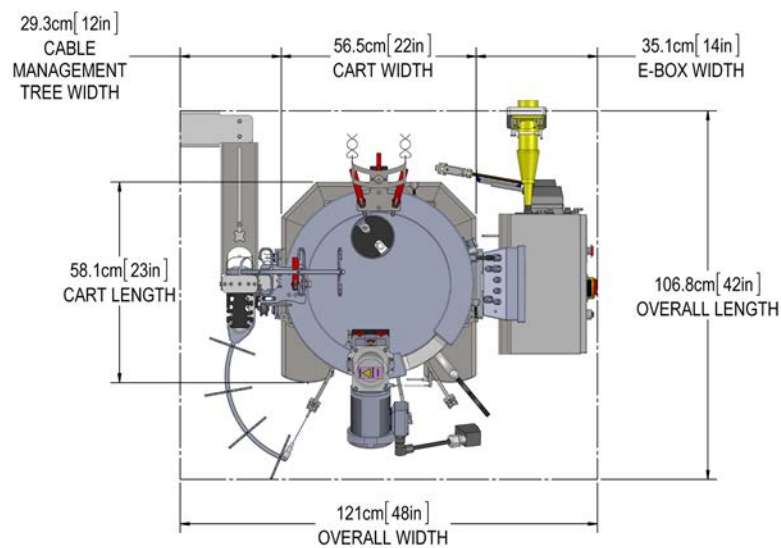


Figure 4.12. Dimensions of 100 L S.U.B. (top view).

Table 4.5. 250 L S.U.B. specifications.

		AC and DC motors
Bioreactor geometry	Rated liquid working volume	250 L
	Minimum liquid working volume	50 L
	Total reactor volume (liquid & gas)	316 L
	BPC chamber diameter	59.7 cm (23.5 in.)
	BPC chamber shoulder height	115.6 cm (45.5 in.)
	Liquid height at rated working volume	91.4 cm (36 in.)
	Fluid geometry at working volume (height/diameter) ratio	1.5:1
	Overall reactor geometry (height/diameter ratio)	1.9:1
	Tank baffles	No
Impeller	Impeller (quantity x blade count)	1 x 3
	Impeller scaling (impeller diameter/tank diameter)	1/3
	Impeller blade pitch (angle)	45°
	Impeller diameter	20 cm (7.875 in.)
	Impeller—calculated power number (N)	2.1
Agitation	Agitation speed range	30–150 ± 1.5 rpm or 1% of setpoint, whichever is greater
	Nominal agitation rating—power/volume ratio	20 W/m ³
	Nominal agitation—20% working volume	69 rpm
	Nominal agitation—50% working volume	93 rpm
	Nominal agitation—100% working volume	117 rpm
	Nominal tip speed	123.6 cm/s (243.3 ft./min.)
	Counterclockwise mixing flow direction	Down-pumping
	Agitation shaft resolved angle	16.5°
	Agitation shaft centerline offset	3.3 cm (1.3 in.)
	Overall drive shaft length	120.90 cm (47.6 in.)
	Drive shaft diameter	1.27 cm (0.5 in.)
	Drive shaft poly-sheath outside diameter	2.54 cm (1 in.)
	Impeller clearance from tank bottom	6.91 cm (2.72 in.)

Table 4.6. 250 L S.U.B. specifications (continued).

		AC motor	DC motor
Motor	Agitation motor drive (type, voltage, phase) AC motor only	Induction, 208 VAC, 3	-
	Agitation motor drive (type, voltage) DC motor only	-	Brushless, 48 VDC
	Motor power rating (AC motor)	186.4 W (0.25 hp)	-
	Motor power rating (DC motor)	-	400 W (0.536 hp)
	Motor torque rating	11.5 Nm (102 in-lb.)	-
	Gear reduction	12.5:1	-
	Programmable VFD, remote panel interface, power faults auto restart	Standard	-
	Motor communication methods (for external controller)	0–10 V, 4–20 mA, Modbus	-
Temperature control	Jacket area: full/half volume	1.26 m ² (13.6 ft. ²) / 0.54 m ² (5.8 ft. ²)	
	Jacket volume	8.6 L	
	Jacket flow rate at 3.4 bar (50 psi)	136 L/min.	
	Process connection	1.5 in. Sanitary tri-clamp	
	Nominal heating/cooling load (W)	2,500 W	
	Approximate liquid heat-up time (5–37°C)—20% volume	1.1 hr	
	Approximate liquid heat-up time (5–37°C)—100% volume	3.4 hr	
	RTD or thermocouple, 3.18 mm (1/8 in.) OD	RTD: Pt-100 (standard)	
Support container	Overall width	112.8 cm (44.4 in.) (with E-box)	68.5 cm (27 in.)
	Overall length	102.2 cm (40.25 in.) (with E-box)	96.9 cm (38.15 in.)
	Overall height	215.5 cm (84.8 in.)	
	Dry skid weight (mass)	223.6 kg (493 lb.)	
	Wet skid weight—rated working volume (mass)	473.6 kg (1044 lb.)	
General	Ceiling height required for drive shaft loading	267.46 cm (105.3 in.)	
	Electrical power supply requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A	Dependent on controller
	pH & DO probe—autoclavable type (Applisens, Broadley James, Mettler Toledo)	12 mm diameter x 215–235 mm insertion length x 13.5 PG thread	
	Noise level	< 70 dB at 1.5 m	
Recommended operating parameters	Operating temperature range	Ambient to 40 +/- 0.5°C (104 +/- 0.9°F)	
	Motor speed	30–150 rpm	
	Volume range	50–250 L	
	Maximum bag pressure	0.03 bar (0.5 psi)	

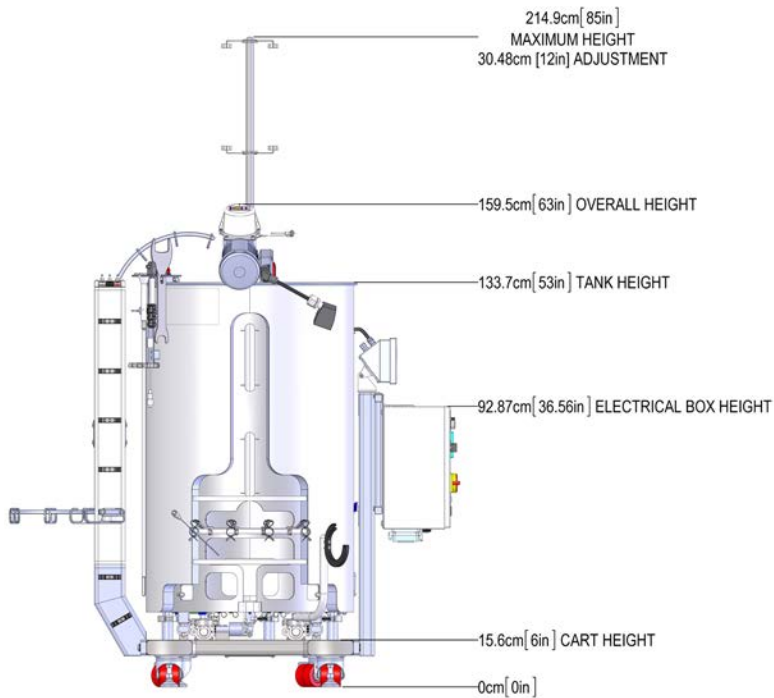


Figure 4.13. Dimensions of 250 L S.U.B. (front view).

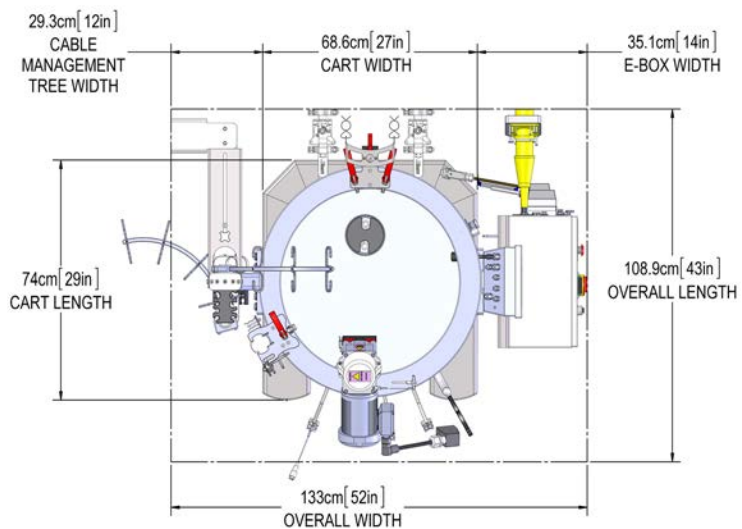


Figure 4.14. Dimensions of 250 L S.U.B. (top view).

Table 4.7. 500 L S.U.B. specifications.

		AC and DC motors
Bioreactor geometry	Rated liquid working volume	500 L
	Minimum liquid working volume	100 L
	Total bioreactor volume (liquid & gas)	660 L
	BPC chamber diameter	75.56 cm (29.75 in.)
	BPC chamber shoulder height	152.4 cm (60 in.)
	Liquid height at rated working volume	113.36 cm (44.63 in.)
	Fluid geometry at working volume (height/diameter) ratio	1.5:1
	Overall bioreactor geometry (height/diameter) ratio	1.9:1
	Tank baffles	No
Impeller	Impeller (quantity x blade count)	1 x 3
	Impeller scaling (impeller diameter/tank diameter)	1/3
	Impeller blade pitch	45°
	Impeller diameter	25.1 cm (9.875 in.)
	Impeller—calculated power number (N)	2.1
Agitation	Agitation speed range	30–150 ± 1.5 rpm or 1% of setpoint, whichever is greater
	Nominal agitation rating (power/volume ratio)	20 W/m ³
	Nominal agitation—20% working volume	59 rpm
	Nominal agitation—50% working volume	80 rpm
	Nominal agitation—100% working volume	101 rpm
	Nominal tip speed	137.2 cm/s (270 ft./min.)
	Counterclockwise mixing flow direction	Down-pumping
	Agitation shaft resolved angle	16.5°
	Agitation shaft centerline offset	5.08 cm (2 in.)
	Overall drive shaft length	155.7 cm (61.3 in.)
	Drive shaft diameter	1.90 cm (0.75 in.)
	Drive shaft poly-sheath outside diameter	2.54 cm (1 in.)
Impeller clearance from tank bottom	7.62 cm (3 in.)	

Table 4.8. 500 L S.U.B. specifications (continued).

		AC motor	DC motor
Motor	Agitation motor drive (type, voltage, phase) AC motor only	Induction, 208 VAC, 3	-
	Agitation motor drive (type, voltage) DC motor only	-	Brushless, 48 VDC
	Motor power rating (AC motor)	372.8 W (0.5 hp)	-
	Motor power rating (DC motor)	-	400 W (0.536 hp)
	Motor torque rating	9.5 Nm (82 in-lb.)	-
	Gear reduction	10:1	-
	Programmable VFD, remote panel interface, power fault auto restart	Standard	-
	Motor communication methods (for external controller)	0–10 V; 4–20 mA; Modbus	-
Temperature control	Jacket area: full/half volume	1.99 m ² (21.4 ft. ²) / 0.78 m ² (8.4 ft. ²)	
	Jacket volume	15.2L	
	Jacket flow rate at 3.4 bar (50 psi)	136 L/min.	
	Process connection	1.5 in. Sanitary tri-clamp	
	Nominal heating/cooling load (W)	5,000 W	
	Approximate liquid heat-up time (5–37°C)—20% volume	1.1 hr	
	Approximate liquid heat-up time (5–37°C)—100% volume	2.2 hr	
	RTD or thermocouple, 3.18 mm (1/8 in.) OD	RTD: Pt-100 (standard)	
Support container	Overall width	125.2 cm (49.3 in.) with E-Box	86.4 cm (34 in.)
	Overall length	124.4 cm (47.8 in.) with E-Box	116 cm (45.7 in.)
	Overall height	251.1 cm (98.9 in.)	
	Dry skid weight (mass)	353.8 kg (780 lb.)	
	Wet skid weight—rated working volume (mass)	853.8 kg (1882.3 lb.)	
General	Ceiling height required for drive shaft loading	282.19 cm (111.1 in.)	
	Electrical power supply requirement (voltage, phase, amp)	120/240 VAC, single, 20/10 A	Dependent on controller
	pH & DO probe—autoclavable type (Applisens, Broadley James, Mettler Toledo)	12 mm diameter x 215–235 mm insertion length x 13.5 PG (pipe) thread	
	Noise level	< 70 dB at 1.5 m	
Recommended operating parameters	Operating temperature range	Ambient to 40 +/- 0.5°C (104 +/- 0.9°F)	
	Motor speed	30–150 rpm	
	Volume range	100–500 L	
	Maximum BPC pressure	0.03 bar (0.5 psi)	

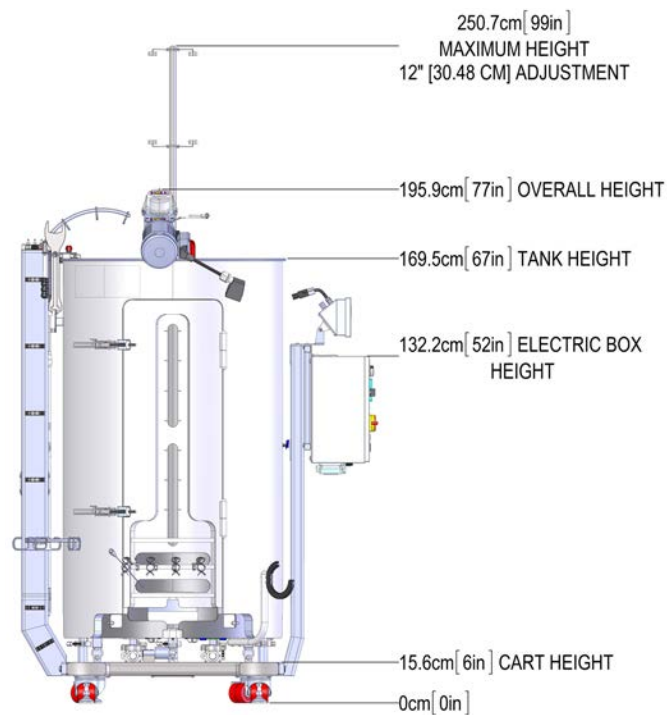


Figure 4.15. Dimensions of 500 L S.U.B. (front view).

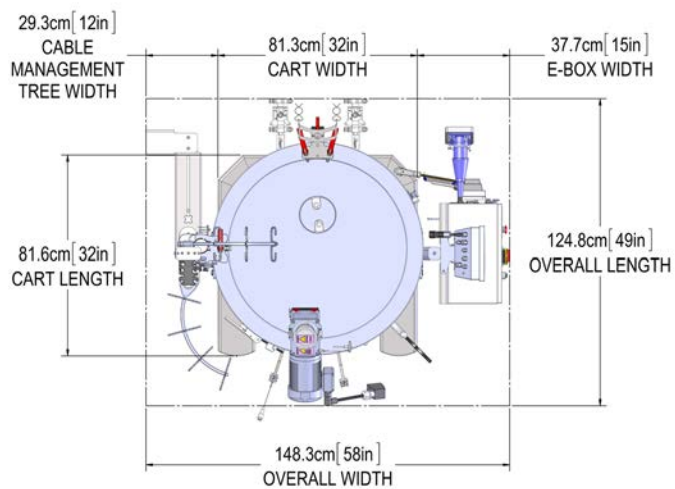


Figure 4.16. Dimensions of 500 L S.U.B. (top view).

Table 4.9. 1,000 L S.U.B. specifications.

Bioreactor geometry	Rated liquid working volume	1,000 L
	Minimum liquid working volume for 5:1 operation	200 L
	Total bioreactor volume (liquid & gas)	1,320 L
	BPC chamber diameter	95.9 cm (37.75 in.)
	BPC chamber shoulder height	200.7 cm (79 in.)
	Liquid height at rated working volume	142.2 cm (56 in.)
	Fluid geometry at working volume (height/diameter) ratio	1.5:1
	Overall bioreactor geometry (height/diameter) ratio	1.9:1
	Tank baffles	No
Impeller	Impeller (quantity x blade count)	1 x 3
	Impeller scaling (impeller diameter/tank diameter)	1/3
	Impeller blade pitch	45°
	Impeller diameter	32.1 cm (12.625 in.)
	Impeller—calculated power number (N)	2.1
Agitation	Agitation speed range for 5:1 operation	20–110 ± 1.5 rpm or 1% of setpoint, whichever is greater
	Nominal agitation rating (power/volume ratio)	20 W/m ³
	Nominal agitation—20% working volume (5:1 operation only)	50 rpm
	Nominal agitation—50% working volume	68 rpm
	Nominal agitation—100% working volume	86 rpm
	Nominal tip speed	146.1 cm/s (287.6 ft./min.)
	Counterclockwise mixing flow direction	Down-pumping
	Agitation shaft resolved angle for 5:1 operation	15.3°
	Agitation shaft centerline offset	5.08 cm (2.0 in.)
	Overall drive shaft length	167.6 cm (66 in.)
	Drive shaft diameter	1.90 cm (0.75 in.)
	Drive shaft poly-sheath outside diameter	3.49 cm (1.375 in.)
	Impeller clearance from tank bottom for 5.1 systems	9.73 cm (3.83 in.)
Motor lift	Power supply requirements	24 VDC, 90 psi of air
	Weight	115.21 kg (254 lb.)

Table 4.10. 1,000 L S.U.B. specifications (continued).

Motor	Agitation motor drive (type, voltage, phase)	Induction, 208 AC, 3
	Motor power rating	372.8 W (0.5 hp)
	Motor torque rating	27.7 Nm (245 in.-lb.)
	Gear reduction	15:1
	Programmable VFD, remote panel interface, power fault auto restart	Standard
	Motor communication methods (for external controller)	0–10 V; 4–20 mA; Modbus
Temperature control	Jacket area: full/half volume	3.31 m ² (35.6 ft. ²) / 1.38 m ² (14.9 ft. ²)
	Jacket volume	23.5 L
	Jacket flow rate at 3.4 bar (50 psi)	136 L/min.
	Process connection	1.5 in. Sanitary tri-clamp
	Nominal heating/cooling load (W)	9,000 W
	Approximate liquid heat-up time (5–37°C)—20% volume	1.2 hr
	Approximate liquid heat-up time (5–37°C)—100% volume	4.1 hr
RTD or thermocouple, 3.18 mm (1/8 in.) OD	RTD: Pt-100 (standard)	
Support container	Overall width	143.8 cm (56.6 in.) with E-Box
	Overall length	139.2 cm (54.8 in.) with E-Box
	Overall height	284 cm (111.8 in.)
	Dry skid weight (mass)	655.01 kg (1,444 lb.)
	Wet skid weight—rated working volume (mass)	1,655.01 kg (3,649 lb.)
General	Ceiling height required for drive shaft loading	287 cm (113 in.)
	Electrical power supply requirement (voltage, phase, amp)	208–240 VAC, single, 30 A/dependent on controller
	pH & DO probe—autoclavable type (Applisens, Broadley James, Mettler Toledo)	12 mm diameter x 215–235 mm insertion length x 13.5 PG (pipe) thread
	Noise level	< 70 dB at 1.5 m
Recommended operating parameters	Operating temperature range	Ambient to 40 +/- 0.5°C (104 +/- 0.9°F)
	Motor speed	20–110 rpm
	Volume range	200–1,000 L
	Maximum BPC pressure	0.03 bar (0.5 psi)

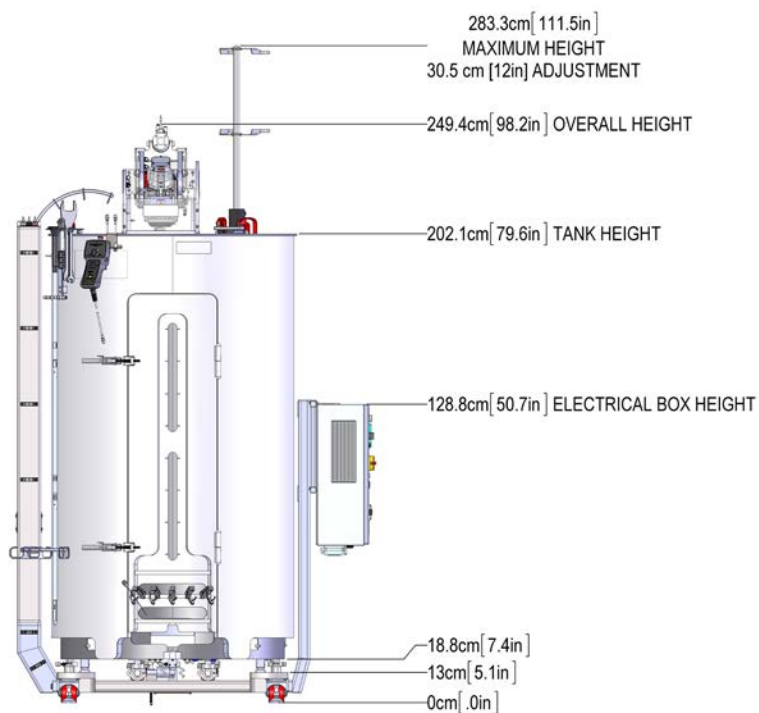


Figure 4.17. Dimensions of 1,000 L S.U.B. (front view).

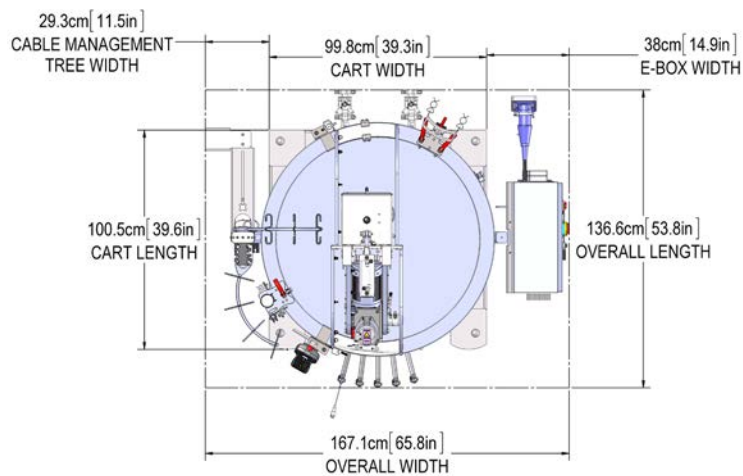


Figure 4.18. Dimensions of 1,000 L S.U.B. (top view).

Table 4.11. 2,000 L S.U.B. specifications.

Bioreactor geometry	Rated liquid working volume	2,000 L
	Minimum liquid working volume for 5:1 operation	400 L
	Total bioreactor volume (liquid & gas)	2,575 L
	BPC chamber diameter	119.4 cm (47 in.)
	BPC chamber shoulder height	229.9 cm (90.5 in.)
	Liquid height at rated working volume	178.7 cm (70.35 in.)
	Fluid geometry at working volume (height/diameter) ratio	1.5:1
	Overall bioreactor geometry (height/diameter) ratio	1.9:1
	Tank baffles	No
Impeller	Impeller (quantity x blade count)	1 x 3
	Impeller scaling (impeller diameter/tank diameter)	1/3
	Impeller blade pitch	45°
	Impeller diameter	39.7 cm (15.67 in.)
	Impeller—calculated power number (N)	2.1
Agitation	Agitation speed range for 5:1 operation	Standard operation: 20–75* ± 1.5 rpm or 1% of setpoint, whichever is greater
	Nominal agitation rating (power/volume ratio)	20 W/m ³
	Nominal agitation—20% working volume (5:1 operation only)	44 rpm
	Nominal agitation—50% working volume	60 rpm
	Nominal agitation—100% working volume	75 rpm
	Minimum acceleration and deceleration rate	60 seconds
	Nominal tip speed	154.9 cm/s (305 ft./min.)
	Counterclockwise mixing flow direction	Down-pumping
	Agitation shaft resolved angle for 5:1 operation	16.6°
	Agitation shaft centerline offset	6.7 cm (2.63 in.)
	Overall drive shaft length	215.6 cm (84.9 in.)
	Drive shaft diameter	1.91 cm (0.75 in.)
	Drive shaft poly-sheath outside diameter	3.51 cm (1.38 in.)
Impeller clearance from tank bottom for 5.1 systems	13.9 cm (5.49 in.)	
General	Ceiling height required for 2-piece drive shaft loading	381 cm (150 in.)
	Ceiling height required for 4-piece drive shaft loading	353.1 cm (139 in.)
	Electrical power supply requirement (voltage, phase, amp)	208–240 VAC, single, 30 A/dependent on controller
	pH & DO probe—autoclavable type (Applisens, Broadley James, Mettler Toledo)	12 mm diameter x 215–235 mm insertion length x 13.5 PG (pipe) thread
	Noise level	< 70 dB at 1.5 m

Table 4.12. 2,000 L S.U.B. specifications (continued).

Motor	Agitation motor drive (type, voltage, phase)	Induction, 208 AC, 3
	Motor power rating	372.8 W (0.5 hp)
	Motor torque rating	27.7 Nm (245 in-lb.)
	Gear reduction	15:1
	Programmable VFD, remote panel interface, power fault auto restart	Standard
	Motor communication methods (for external controller)	0–10 V; 4–20 mA; Modbus
Temperature control	Jacket area: full/half volume	4.54 m ² (48.9 ft. ²) / 2.47 m ² (26.6 ft. ²)
	Jacket volume	44 L
	Jacket flow rate at 3.4 bar (50 psi)	75 L/min.
	Process connection	1.5 in. Sanitary tri-clamp
	Nominal heating/cooling load (W)	18,000 W
	Approximate liquid heat-up time (5–37°C)—20% volume	1.4 hr
	Approximate liquid heat-up time (5–37°C)—100% volume	4 hr
RTD or thermocouple, 3.18 mm (1/8 in.) OD	RTD: Pt-100 (standard)	
Support container	Overall width	179.7 cm (70.5 in.) with E-Box
	Overall length	171.4 cm (67.5 in.)
	Overall height	321.1 cm (126.4 in.)
	Dry skid weight (mass)	962.1 kg (2,121 lb.)
	Wet skid weight—rated working volume (mass)	2,962.1 kg (6,530 lb.)
Recommended operating parameters	Operating temperature range	Ambient to 40 +/- 0.5°C (104 +/- 0.9°F)
	Motor speed	Standard operation: 20–75* rpm, working volumes must stay above 50% during agitation
	Volume range	400–2,000 L
	Maximum BPC pressure	0.03 bar (0.5 psi)
BPC lift	Electrical power supply requirement	120–240 VAC, 50/60 Hz, 10 A
	Duty cycle for motor	Tested to 5 cycles/10 minutes
Motor lift	Power supply requirements	24 VDC, 90 psi of air
	Weight	126.1 kg (278 lb.)

* **WARNING:** Mixing speeds must stay within the recommended operating parameters. Higher speed operation compromises system reliability and will void standard Thermo Fisher warranties. Your control strategy should include governors that regulate rpm based on liquid volume as well as safety interlocks that disable mixing when the liquid drops below the recommended volume. See section 3.6.5 for more information about operating parameters, agitation speed governors, and safety interlocks.

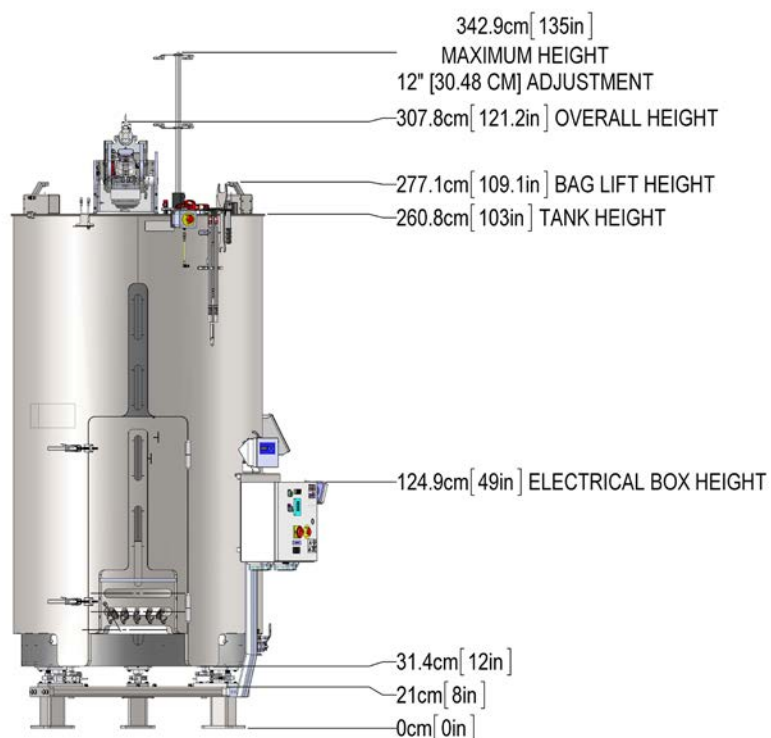


Figure 4.19. Dimensions of 2,000 L S.U.B. (front view).

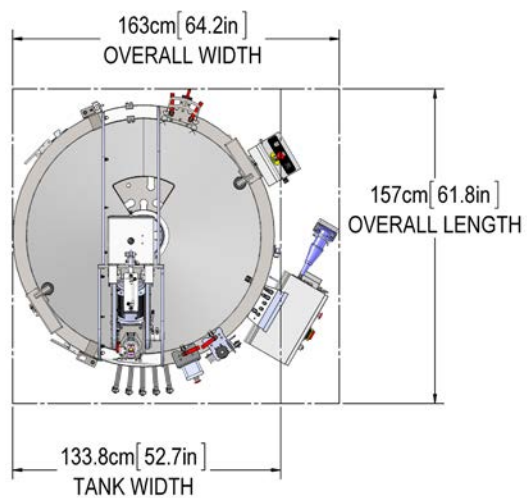


Figure 4.20. Dimensions of 2,000 L S.U.B. (top view).

4.3. E-Box features

Figure 4.21 illustrates the features of the E-Box available for 50 L, 100 L, 250 L, 500 L, 1,000 L, and 2,000 L S.U.B. units with AC motors. Figure 4.22 illustrates the bottom view of the E-Box.



Figure 4.21. Front view of the E-Box for 50–2,000 L S.U.B.s.

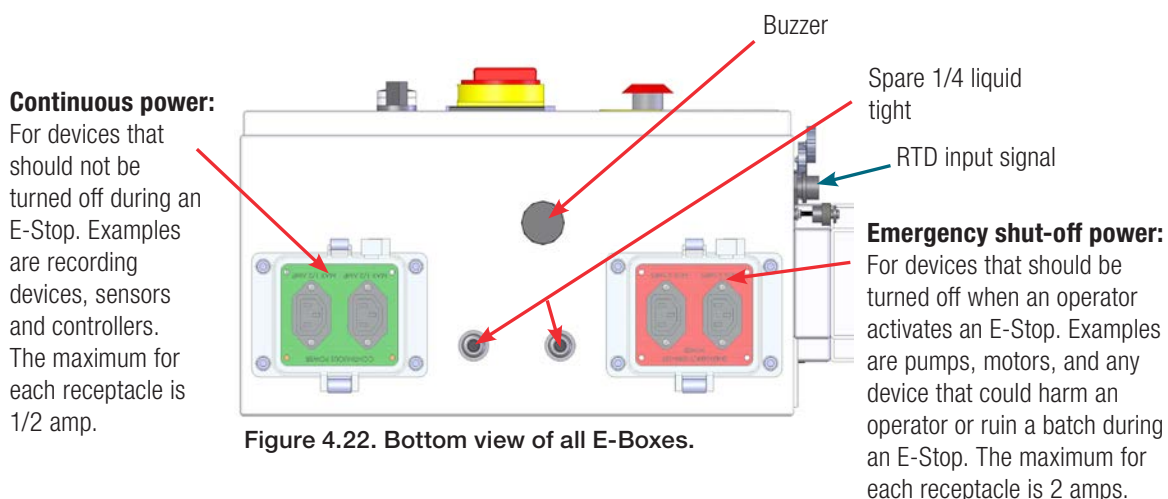


Figure 4.22. Bottom view of all E-Boxes.

4.4. BPC specifications

The following figures and tables provide specification information for 5.1 BPCs in 50, 100, 250, 500, 1,000, and 2,000 L sizes.

5.1 S.U.B. 50 L BPC with AseptiQuik connector ports

Specification information for the numbered items in Figure 4.23 is located in Table 4.13 on the following page.

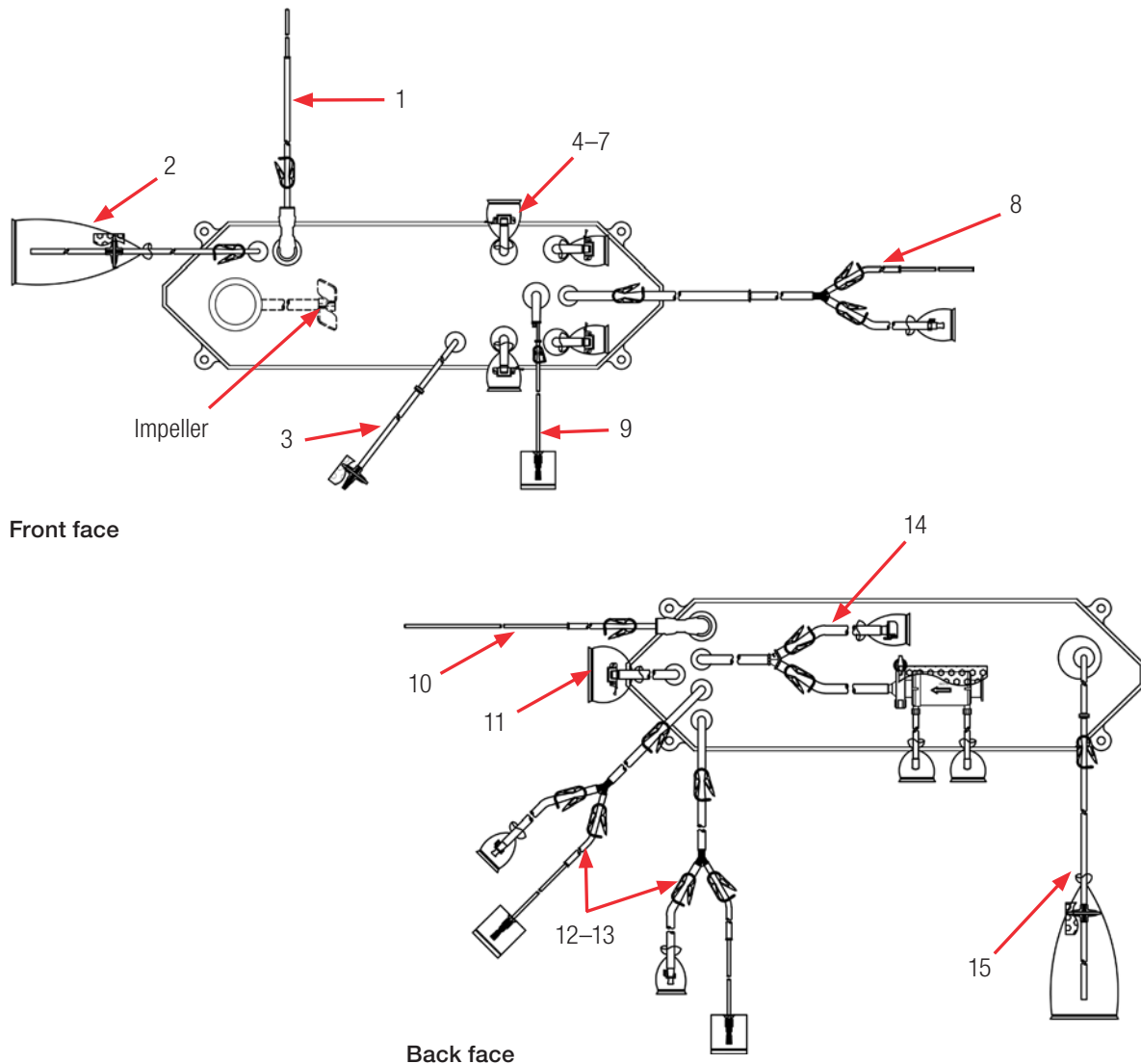


Figure 4.23. Front and back faces of 50 L S.U.B. BPC.

Table 4.13. 50 L BPC specification information.

Item	Description	Tubing set (ID x OD x length)	End treatment
1	Inoculum addition	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 152 cm (60 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.)	Plugged
2	Overlay gas sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.)	Hydrophobic vent filter with Emflon II, connected to 15 cm (6 in.) C-Flex tubing
3	Cross flow sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 183 cm (72 in.)	Meissner Steridyne 50 mm (1.97 in.) filter
4–7	Probe ports (4)	12.7 mm (1/2 in.) tube ports	CPC AseptiQuik aseptic connectors
8	Bottom drain harvest	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 152 cm (60 in.) Reduced to 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.) Splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex Tubing x 30 cm (12 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	Plugged and 9.5 mm (3/8 in.) MPC insert
9	Thermowell/ small volume sample	Thermowell adapter for 3.2 mm (1/8 in.) diameter RTD and 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 46 cm (18 in.)	Luer lock and SterilEnz pouch with injection site assembly
10	Base addition	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 152 cm (60 in.)	Plugged
11	Pressure sensor port	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 8 cm (3 in.)	CPC AseptiQuik aseptic connector
12–13	Feed lines	9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 152 cm (60 in.) Splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	SteriEnz pouch with injection site assembly and 9.5 mm (3/8 in.) MPC body
14	Exhaust line	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 20 cm (8 in.) Connected to 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 15 cm (6 in.) and 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 25 cm (10 in.)	CPC AseptiQuik aseptic connector— Pall Kleenpak 0.2 micron exhaust vent filter
15	Drilled hole sparger 8.9 cm (3.5 in.) disk with 360 x 0.178 mm (0.007 in.) holes	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) Connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 97 cm (38 in.)	Meissner Steridyne 0.2 micron hydrophobic filter connected to 15 cm (6 in.) C-Flex

5.1 S.U.B. 100 L BPC with AseptiQuik connector ports

Specification information for the numbered items in Figure 4.24 is located in Table 4.14 on the following page.

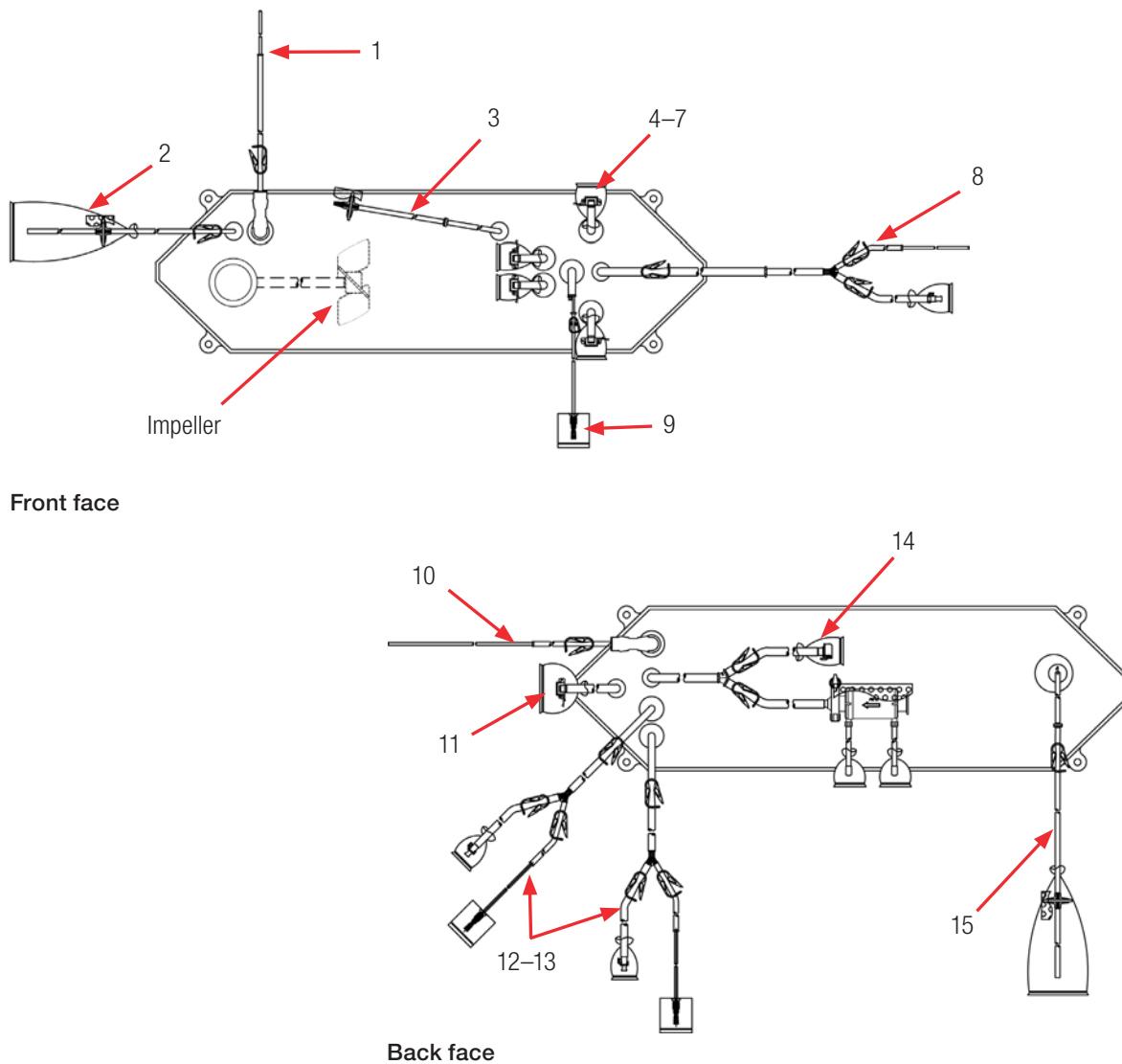


Figure 4.24. Front and back faces of 100 L S.U.B. BPC.

Table 4.14. 100 L BPC specification information.

Item	Description	Tubing set (ID x OD x length)	End treatment
1	Inoculum addition	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 152 cm (60 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.)	Plugged
2	Overlay gas sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 20 cm (8 in.)	Hydrophobic vent filter with Emflon II, connected to 15 cm (6 in.) C-Flex tubing
3	Cross flow sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 183 cm (72 in.)	Meissner Steridyne 50 mm (1.97 in.) filter
4–7	Probe ports (4)	12.7 mm (1/2 in.) tube ports	CPC AseptiQuik aseptic connectors
8	Bottom drain harvest	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 152 cm (60 in.) Reduced to 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.) Splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	Plugged and 9.5 mm (3/8 in.) MPC insert
9	Thermowell/ small volume sample	Thermowell adapter for 6.4 mm (1/4 in.) diameter RTD and 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 46 cm (18 in.)	SteriEnz pouch with injection site assembly
10	Base addition	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 152 cm (60 in.)	Plugged
11	Pressure sensor port	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 8 cm (3 in.)	CPC AseptiQuik aseptic connector
12–13	Feed lines	9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 152 cm (60 in.) Splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	SteriEnz pouch with injection site assembly and 9.5 mm (3/8 in.) MPC body
14	Exhaust line	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 20 cm (8 in.) Connected to 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 15 cm (6 in.) and 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 25 cm (10 in.)	CPC AseptiQuik aseptic connector— Pall Kleenpak 0.2 micron exhaust vent filter
15	Drilled hole sparger 8.9 cm (3.5 in.) disk with 570 x 0.178 mm (0.007 in.) holes	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) Connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 114 cm (45 in.)	Meissner Steridyne 0.2 micron hydrophobic filter connected to 15 cm (6 in.) C-Flex

5.1 S.U.B. 250 L BPC with AseptiQuik connector ports

Specification information for the numbered items in Figure 4.25 is located in Table 4.15 on the following page.

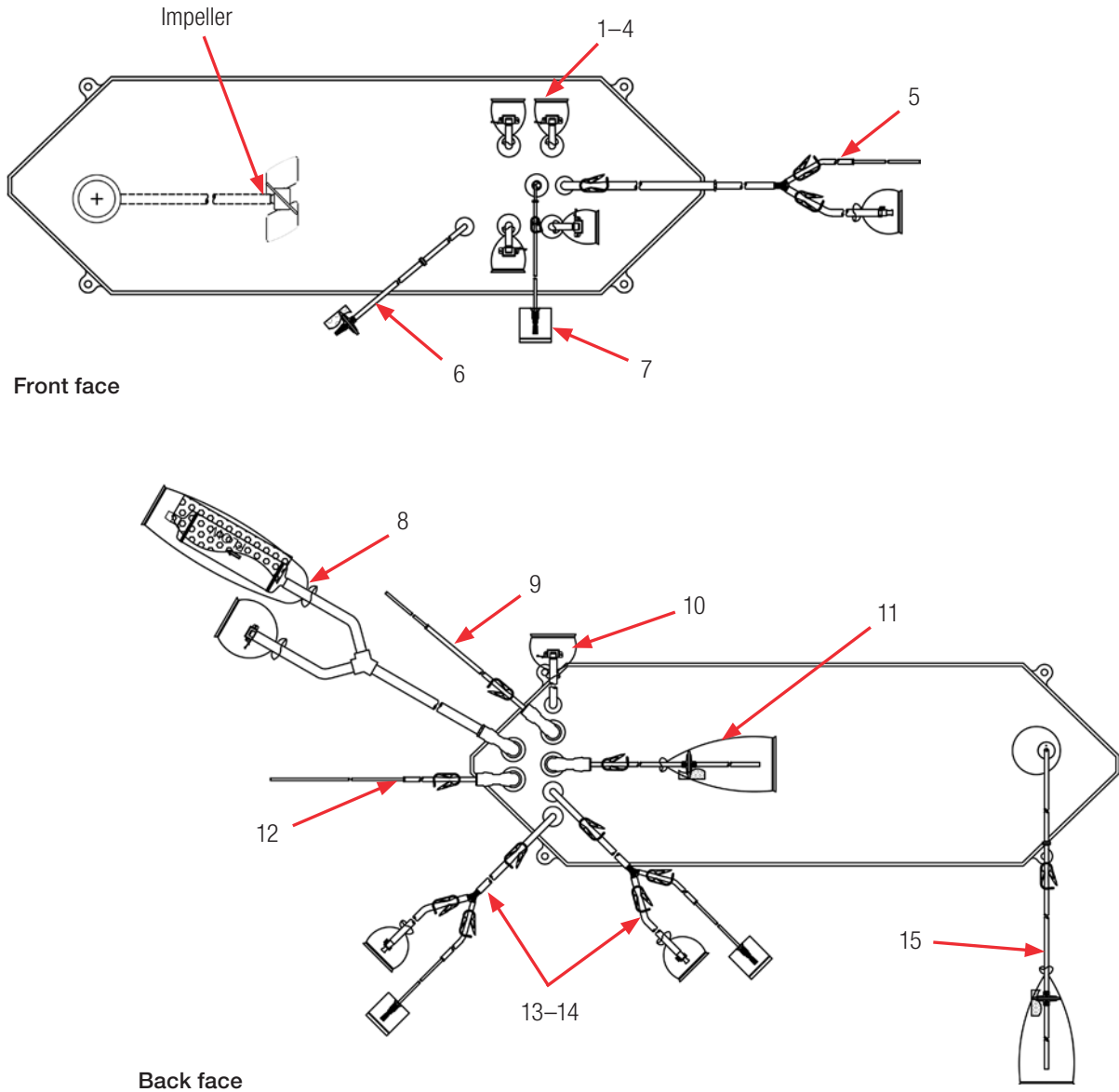


Figure 4.25. Front and back faces of 250 L S.U.B. BPC.

Table 4.15. 250 L BPC specification information.

Item	Description	Tubing set (ID x OD x length)	End treatment
1–4	Probe ports (4)	12.7 mm (1/2 in.) tube ports	CPC AseptiQuik aseptic connectors
5	Bottom drain harvest	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 152 cm (60 in.) Reduced to 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.) Splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	Plugged and 9.5 mm (3/8 in.) MPC insert
6	Cross flow sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 183 cm (72 in.)	Meissner Steridyne 50 mm (1.97 in.) filter
7	Thermowell/ small volume sample	Thermowell adapter for 6.4 mm (1/4 in.) diameter RTD and 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 46 cm (18 in.)	SterilEnz pouch with injection site assembly
8	Exhaust line	19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 30 cm (12 in.) Splits to 19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 15 cm (6 in.) and 19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 15 cm (6 in.)	CPC AseptiQuik aseptic connector, (2) Meissner Ultracap 0.2 micron hydrophobic filters
9	Inoculum addition	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 152 cm (60 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm 1/4 in.) C-Flex tubing x 30 cm (12 in.)	Plugged
10	Pressure sensor port	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 8 cm (3 in.)	CPC AseptiQuik aseptic connector
11	Overlay gas sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.)	Meissner Steridyne 0.2 micron hydrophobic filter connected to 15 cm (6 in.) C-Flex
12	Base addition	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 152 cm (60 in.)	Plugged
13–14	Feed lines	9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 152 cm (60 in.) Splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	SteriEnz pouch with injection site assembly and 9.5 mm (3/8 in.) MPC body
15	Drilled hole sparger 12.2 cm (4.8 in.) disk with 760 x 0.233 mm (0.009 in.) holes	6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) Connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) OD C-Flex tubing x 150 cm (59 in.)	Meissner Steridyne 0.2 micron hydrophobic filter connected to 15 cm (6 in.) C-Flex

5.1 S.U.B. 500 L BPC with AseptiQuik connector ports

Specification information for the numbered items in Figure 4.26 is located in Table 4.16 on the following page.

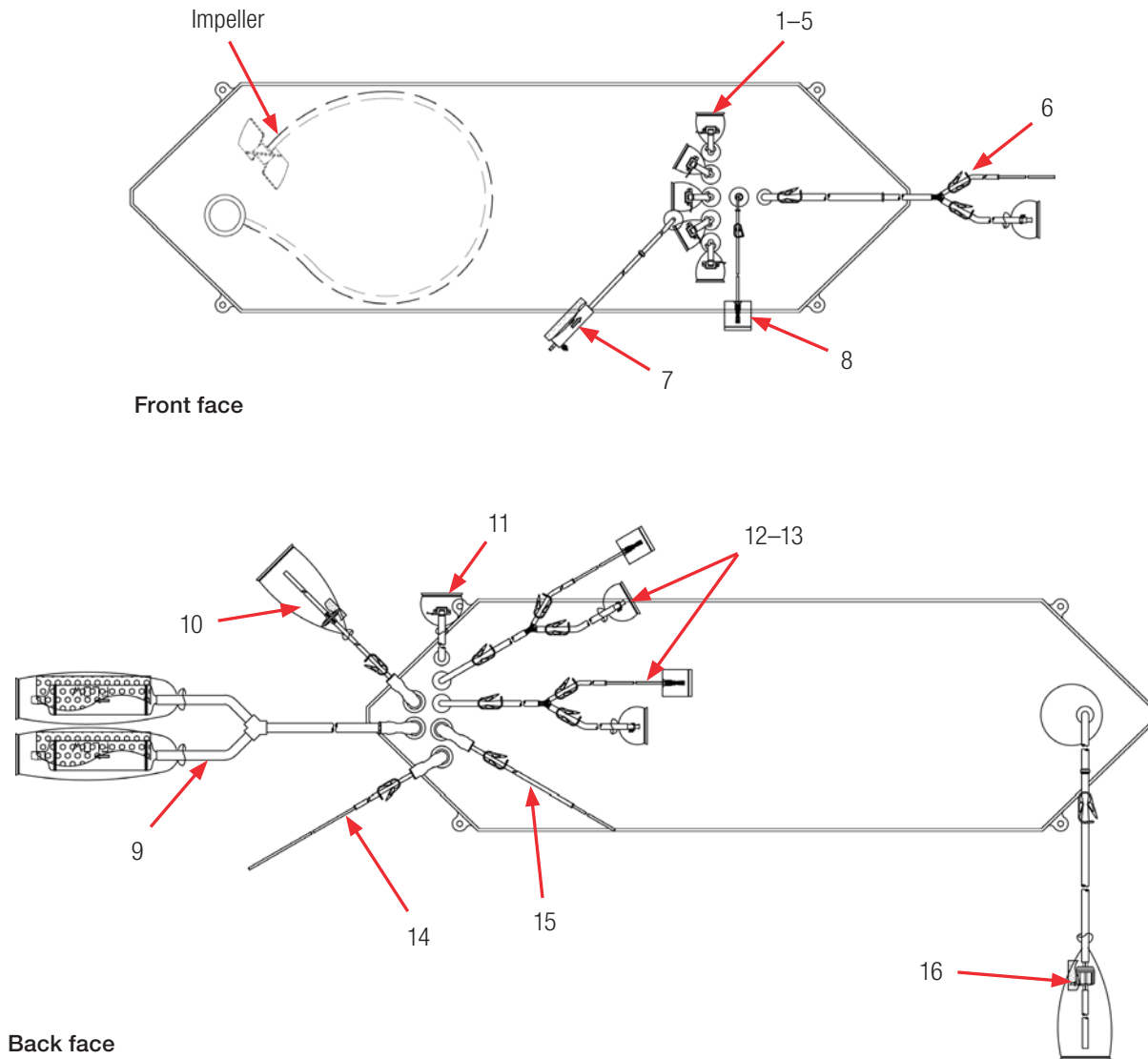


Figure 4.26. Front and back faces of 500 L S.U.B. BPC.

Table 4.16. 500 L BPC specification information.

Item	Description	Tubing set (ID x OD x length)	End treatment
1–5	Probe ports (4)	12.7 mm (1/2 in.) tube ports	CPC AseptiQuik aseptic connectors
6	Bottom drain harvest	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 152 cm (60 in.) Reduced to 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.) Splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	Plugged and 9.5 mm (3/8 in.) MPC insert
7	Cross flow sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 183 cm (72 in.)	Meissner Steridyne 50 mm (1.97 in.) filter
8	Thermowell/ small volume sample	Thermowell adapter for 6.4 mm (1/4 in.) diameter RTD and 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 46 cm (18 in.)	SteriEnz pouch with injection site assembly
9	Exhaust line	19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 30 cm (12 in.) Splits to 19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 15 cm (6 in.) and 19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 15 cm (6 in.)	Meissner Ultracap 0.2 micron hydrophobic filters
10	Overlay gas sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.)	Hydrophobic vent filter with Emflon II, connected to 15 cm (6 in.) C-Flex
11	Pressure sensor port	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 8 cm (3 in.)	CPC AseptiQuik aseptic connector
12–13	Feed lines	9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 213 cm (84 in.) Splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	SteriEnz pouch with injection site assembly and 9.5 mm (3/8 in.) MPC body
14	Base addition	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 213 cm (84 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.)	Plugged
15	Inoculum addition	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 213 cm (84 in.)	Plugged
16	Drilled hole sparger 17.14 cm (6.75 in.) disk with 980 x 0.368 mm (0.014 in.) holes	6.4 mm (1/4 in.) ID x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) Connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) OD C-Flex tubing x 97 cm (38 in.)	Kleenpak Emflon 0.2 micron hydrophobic filter connected to 15 cm (6 in.) C-Flex

5.1 S.U.B. 1,000 L BPC with AseptiQuik connector ports

Specification information for the numbered items in Figure 4.27 is located in Table 4.17 on the following page.

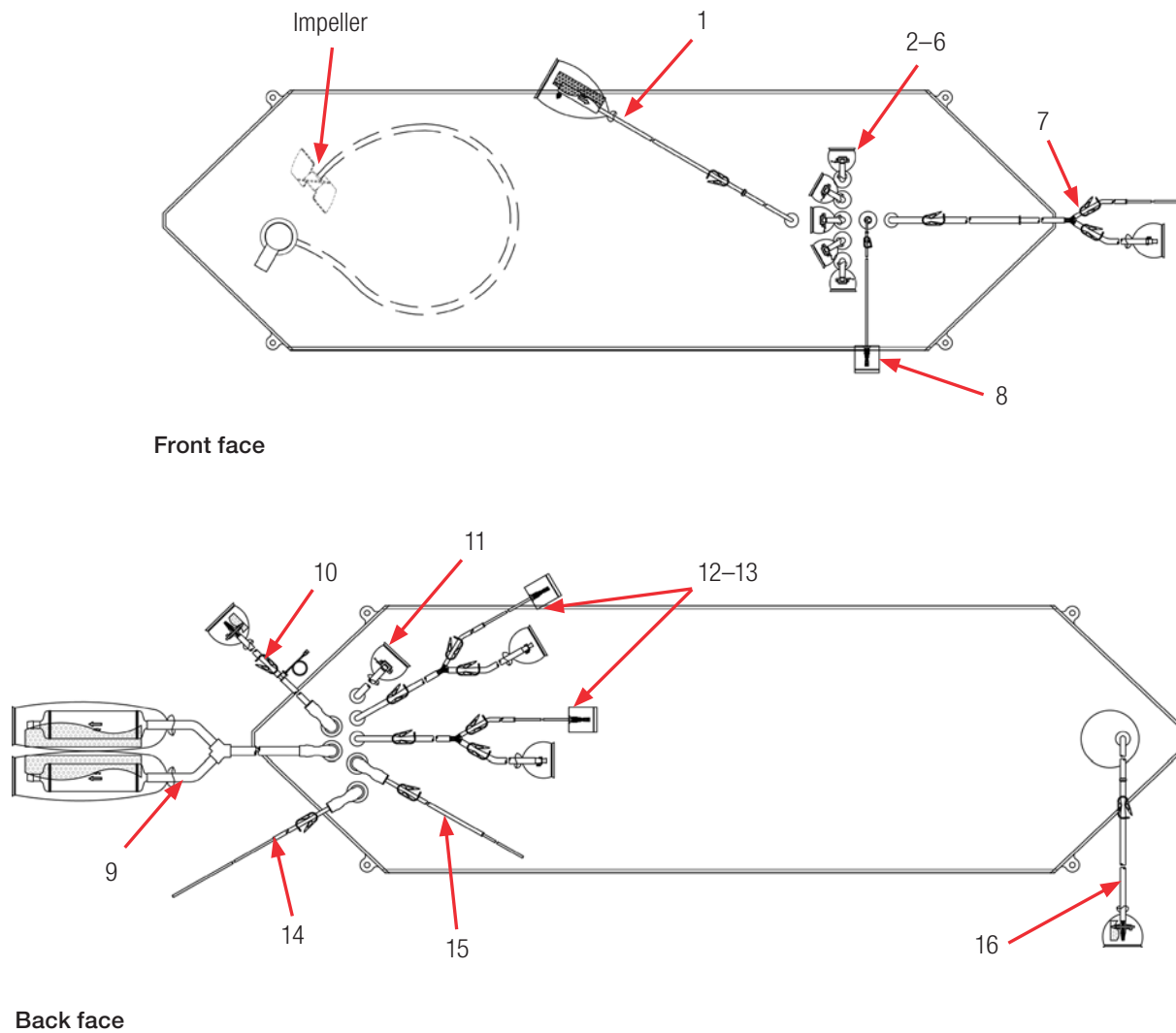


Figure 4.27. Front and back faces of 1,000 L S.U.B. BPC.

Table 4.17. 1,000 L BPC specification information.

Item	Description	Tubing set (ID x OD x length)	End treatment
1	Cross flow sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 183 cm (72 in.)	Meissner Steridyne 50 mm (1.97 in.) filter
2–6	Probe ports (4)	12.7 mm (1/2 in.) tube ports	CPC AseptiQuik aseptic connectors
7	Bottom drain harvest	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 152 cm (60 in.) Reduced to 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.) Splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	Plugged and 9.5 mm (3/8 in.) MPC insert
8	Thermowell/ small volume sample	Thermowell adapter for 6.4 mm (1/4 in.) diameter RTD and 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 60 cm (24 in.)	SteriEnz pouch with injection site assembly
9	Exhaust line	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 30 cm (12 in.) Splits to 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 15 cm (6 in.) and 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 15 cm (6 in.)	(2) Meissner Ultracap 0.2 micron hydrophobic filters connected to 15 cm (6 in.) C-Flex tubing
10	Overlay gas sparger	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 10 cm (4 in.) Reduced to 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 213 cm (84 in.)	Kleenpak Emflon II capsule and pressure transducer
11	Pressure sensor port	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 8 cm (3 in.)	CPC AseptiQuik aseptic connector
12–13	Feed lines	9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 213 cm (84 in.) Splits to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 30 cm (12 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.) and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 30 cm (12 in.)	SteriEnz pouch with injection site assembly and 9.5 mm (3/8 in.) MPC body
14	Base addition	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 213 cm (84 in.)	Plugged
15	Inoculum addition	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 213 cm (84 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.)	Plugged
16	Drilled hole sparger 17.1 cm (6.75 in.) disk with 1,180 x 0.445 mm (0.018 in.) holes	9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 8 cm (3 in.) Connected to check valve and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 264 cm (97 in.)	Meissner Steridyne 0.2 micron hydrophobic filter connected to 15 cm (6 in.) C-Flex

5.1 S.U.B. 2,000 L BPC with AseptiQuik connector ports

Specification information for the numbered items in Figure 4.28 is located in Table 4.18 on the following page.

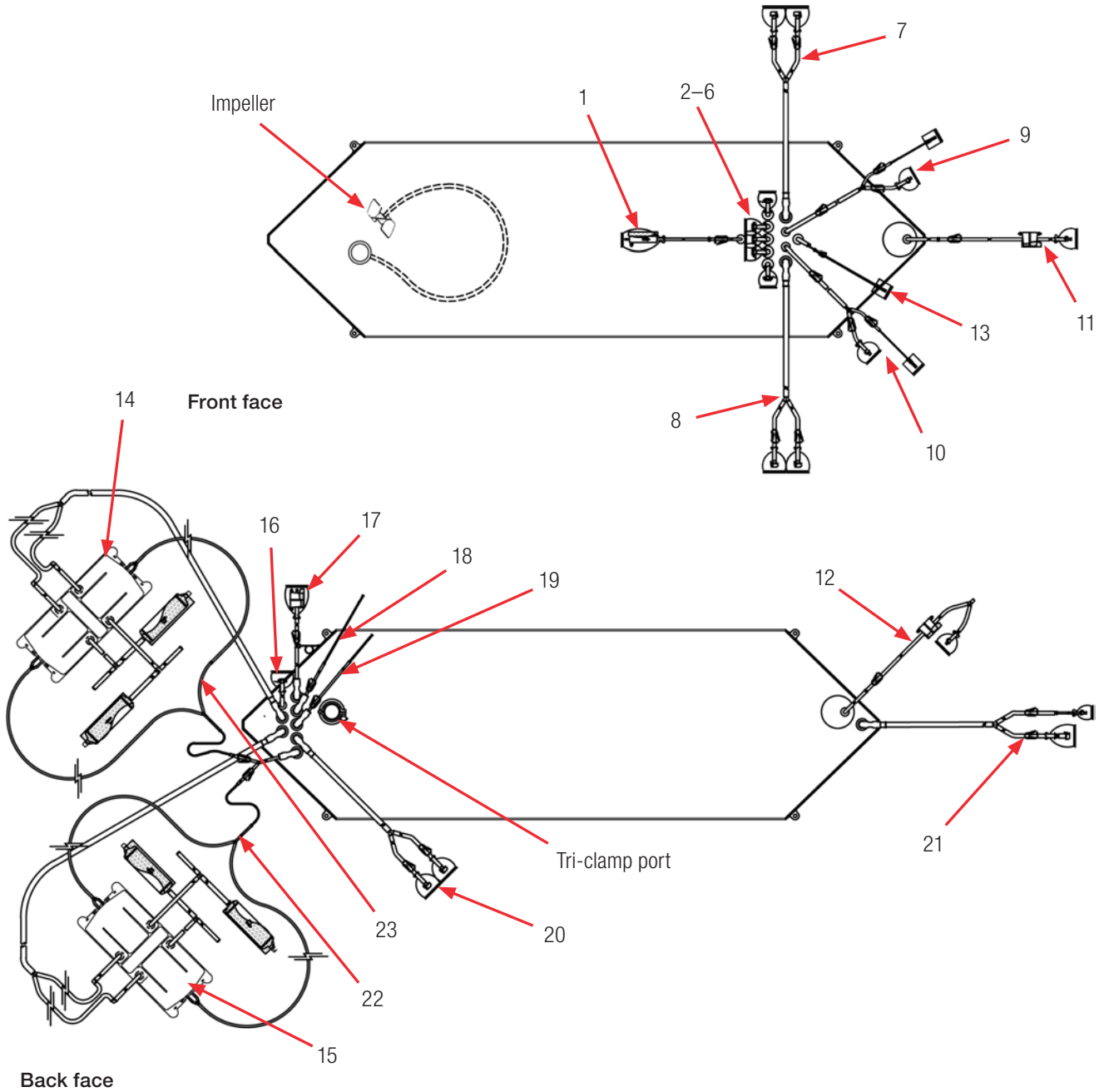


Figure 4.28. Front and back faces of 2,000 L S.U.B. BPC.

Table 4.18. 2,000 L BPC specification information.

Item	Description	Tubing set (ID x OD x length)	End treatment
1	Cross flow sparger	6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 8 cm (3 in.) connected to check valve and 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 183 cm (72 in.)	Meissner Steridyne 50 mm (1.97 in.) filter
2–6	Probe ports (5)	12.7 mm (1/2 in.) tube ports	CPC AseptiQuik aseptic connectors
7–8	Media fill/ auxiliary drain lines (2)	19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 213 cm (84 in.) splits to 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 61 cm (24 in.) and 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 61 cm (24 in.)	CPC AseptiQuik aseptic connectors
9–10	Feed lines (2)	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 10 cm (4 in.) Splits to 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 25 cm (10 in.) and 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 25 cm (10 in.)	SterilEnz pouch with injection site assembly and 9.5 mm (3/8 in.) MPC body
11–12	Drilled hole sparger 17.1 cm (6.75 in.) disk with 1,380 (690 x 0.582 mm) (0.023 in.) holes	9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 8 cm (3 in.) Connected to check valve and 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 183 cm (72 in.)	Meissner Steridyne 0.2 micron hydrophobic filter with 9.5 mm (3/8 in.) C-Flex tubing (Y-connector and quick-connects provided for joining lines)
13	Thermowell/ small volume sample port	Thermowell adapter for 6.4 mm (1/4 in.) diameter 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 61 cm (24 in.)	SterilEnz pouch with injection site assembly
14–15	Condenser bag assemblies (2)	Condenser bag assembly (optional)	–
16	Pressure sensor port	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 8 cm (3 in.)	CPC AseptiQuik aseptic connectors
17	Overlay gas sparger	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 10 cm (4 in.) Reduced to 9.5 mm (3/8 in.) x 15.9 mm (5/8 in.) C-Flex tubing x 213 cm (84 in.)	Kleenpak Emflon II capsule and pressure transducer
18	Inoculum addition	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 8 cm (3 in.) Reduced to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 15 cm (6 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 213 cm (84 in.)	Plugged
19	Base addition	12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 8 cm (3 in.) Reduced to 6.4 mm (1/4 in.) x 11.1 mm (7/16 in.) C-Flex tubing x 213 cm (84 in.) Reduced to 3.2 mm (1/8 in.) x 6.4 mm (1/4 in.) C-Flex tubing x 30 cm (12 in.)	Plugged
20	Media fill/ auxiliary drain line	19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 213 cm (84 in.) splits to 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 61 cm (24 in.) and 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 61 cm (24 in.)	CPC AseptiQuik aseptic connectors
21	Bottom drain harvest	19.1 mm (3/4 in.) x 25.4 mm (1 in.) C-Flex tubing x 122 cm (48 in.) splits to 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 61 cm (24 in.) reduced to 6.4 mm (1/4 in.) x 9.5 mm (3/8 in.) C-Flex tubing x 30 cm (12 in.) and 12.7 mm (1/2 in.) x 19.1 mm (3/4 in.) C-Flex tubing x 61 cm (24 in.)	1/4 in. MPC insert and Kleenpak (male)
22	Exhaust lines (2)	Condenser bag assembly (optional)	–
23	Condensate return line	Condenser bag assembly (optional)	–

BPC packing information

Standard 5.1 S.U.B. BPC packaging is listed in Table 4.19, below.

Table 4.19. Standard 5.1 BPC packaging.

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

4.5. Additional system component part numbers

The following tables list part numbers for additional 5.1 S.U.B. system components, such as drive shafts, load cell kits, and accessories.

Table 4.20. Drive shaft part numbers.

Description	Cat. no.
50 L 1-piece aluminum drive shaft	SV50959.10
100 L 1-piece aluminum drive shaft	SV50959.18
250 L 1-piece stainless steel drive shaft	SV50959.11
500 L 2-piece stainless steel drive shaft	SV50959.12
1,000 L 3-piece stainless steel drive shaft	SV50177.38
1,000 L 4-piece stainless steel drive shaft	SV50177.39
2,000 L 2-piece carbon fiber drive shaft	SV50959.21
2,000 L 4-piece carbon fiber drive shaft	SV50959.20

Table 4.21. Cable management system part numbers.

Description	Cat. no.
50 L and 100 L S.U.B. cable management system	SV50992.01
250 L S.U.B. cable management system	SV50992.02
500 L S.U.B. cable management system	SV50992.03
1,000 L S.U.B. cable management system	SV50992.04

Table 4.22. Load cell part numbers. 1,000 L and 2,000 L S.U.B.s include load cells as standard equipment. The following kits are for retro-fitting to 50 L, 100 L, 250 L, and 500 L S.U.B. systems.

Description	Cat. no.
50–100 L S.U.B. load cell kit with summing block, no display	SV50988.01
250 L S.U.B. load cell kit with summing block, no display	SV50988.02
500 L S.U.B. load cell kit with summing block, no display	SV50988.03

Table 4.23. Harsh mount load cell display part numbers for 50–500 L and 2,000 L systems.

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

Table 4.24. Vent filter heater kit part numbers for use with Pall KA3 vent filters. Includes vent filter heater, controller with water-tight closure, quick-connects, and installation power cord.

Description	Cat. no.
NEMA rated vent heater with programmable controller (100–120 VAC), power cord. Includes low-temp. alarm, preset temp. 50°C, and power cord with flying leads.	SV50191.11
NEMA rated vent heater with programmable controller (200–240 VAC), power cord. Includes low temp. alarm, preset temp. 50°C, and power cord with flying leads.	SV50191.13

Table 4.25. Vent filter heater kit part numbers for use with Meissner Ultracap 10 inch vent filters. Includes vent filter heater, controller with water-tight closure, quick-connects, and installation power cord.

Description	Cat. no.
NEMA rated vent heater with programmable controller (100–120 VAC). Includes low-temp. alarm, preset temp. 50°C, and 20 ft. NEMA 5-15 power cord for US/Japan.	SV50191.16
NEMA rated vent heater with programmable controller (200–240 VAC). Includes low temp. alarm, preset temp. 50°C, and 20 ft. BS1363 power cord for UK.	SV50191.17
NEMA rated vent heater with programmable controller (200–240 VAC). Includes low temp. alarm, preset temp. 50°C, and 20 ft. CEE7/7 power cord for Europe.	SV50191.18
NEMA rated vent heater with programmable controller (200–240 VAC). Includes low temp. alarm, preset temp. 50°C, and 12 ft. IEC320 power cord for 2,000 L S.U.B. control box.	SV50191.19

Table 4.26. Condenser system part numbers (for 2,000 L systems only).

Description	Cat. no.
Condenser system (120 V) including cart, chill plate and mounting post with filter brackets, TCU, and pump	SV50232.01
Condenser system (240 V) including cart, chill plate and mounting post with filter brackets, TCU, and pump	SV50232.02

Table 4.27. AC and DC motor part numbers.

Description	Cat. no.
50 L, 100 L, and 250 L S.U.B. DC motor	SV50237.07
50 L, 100 L, and 250 L S.U.B. AC motor	SV50237.16
500 L, 1,000 L, and 2,000 L S.U.B. DC motor	SV50237.22
500 L S.U.B. AC motor	SV50237.18
1,000 L and 2,000 L S.U.B. AC motor	SV50237.19

Table 4.28. Miscellaneous and accessory part numbers.

Component	Cat. no.
Probe assembly with CPC AseptiQuik connector (non-sterile, for use in autoclave)	SH30720.02
Probe assembly with Pall Kleenpak connector (non-sterile, for use in autoclave)	SH30720.01
Heavy-duty tubing clamp	SV20664.01
Stainless steel autoclave tray, for autoclaving probe assemblies	SV50177.01
Probe clips	SV50177P.01
Sterile sampling manifold with luer lock	SH30845.01
Temperature/sample port	SV20750.01
Sparge line support	SV50177.19
Mobile stairs (for 2,000 L systems only)	SV50935.01

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

High-wear items such as bearings, seals, O-rings, and sterilization valves common to conventional bioreactor systems have been purposefully considered in the design of the construction of the S.U.B. The S.U.B. system is inherently robust and requires low levels of routine maintenance. Taking time between bioreactor runs to clean the exterior of the hardware will improve the appearance and overall longevity of the system. The drive motor is an industrial grade induction motor with a permanently sealed and lubricated gear box. The drive shaft is constructed to wear slightly with use and should be visually inspected after each run. Visual inspection of wear components and following the guidelines listed below will be sufficient to ensure dependable service. Replacement parts are available.

5.1.2. Preventive maintenance

- Lightly coat the drive cap threads with food-grade anti-seize if the motor cap becomes difficult to turn.
- For multiple-segment drive shafts without quick-connects, lightly coat the threads with food-grade anti-seize during assembly.
- Replacement of the mixing motor is recommended every five years, or as needed.
- Refer to the following section of this user's guide for expected drive shaft longevity based on usage.

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 the widest location across the points.

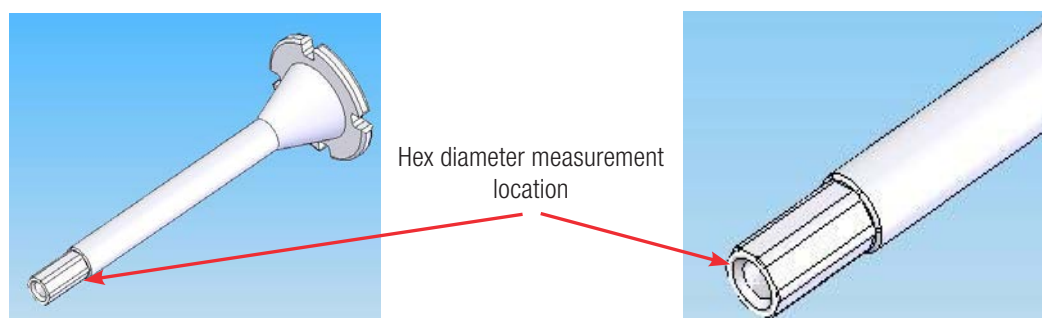


Figure 5.1. Shaft head assembly.

Under normal operating conditions, replace the drive shaft assembly after 360 days of service, or refer to the drive shaft head wear specifications in Table 5.1, below.

Table 5.1. Drive shaft head hex diameters.

S.U.B. system	New hex diameter	Minimum hex diameter
50, 100 and 250 L	14.9 mm (0.587 in.) +/- 0.127 mm	14.4 mm (0.566 in.)
500 and 1,000 L	21.3 mm (0.839 in.) +/- 0.127 mm	20.8 mm (0.820 in.)

Drive shaft longevity and replacement

For 50 L, 100 L, 250 L, 500 L, and 1,000 L S.U.B. systems, we recommend replacing your drive shaft every 360 days of cumulative use.

2,000 L S.U.B. systems experience a greater amount of fatigue-related stress than smaller systems due to the use of a longer drive shaft. If you are operating a 2,000 L S.U.B. at a P/V ratio of 20 W/m^3 , replace your drive shaft every 180 days of cumulative use. If you are operating a 2,000 L S.U.B. at 40 W/m^3 , consultation with Thermo Scientific engineers is required. For more information on the use of P/V ratios, see section 3.6.5 of this publication. **Note:** Operating 2,000 L systems below 50% working volume requires the use of safety interlocks and speed governors. See the Warnings, safety, and warranty information section in the front of this publication for more information.

Note: For warranty purposes, drive shaft use must be documented. A drive shaft use log is provided in Appendix D of this publication.

5.2. Troubleshooting and frequently asked questions

5.2.1. Hardware operation issues

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

Solution: **Check the power supply.**

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

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

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

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

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

Solution: **No action is required.**

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

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

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

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

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

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

Issue: **How do we ensure that we are using the correct components and setting up the S.U.B. properly for 5:1 mixing?**

Solution: **Before you begin setup, verify that all hardware and components are labeled for 5:1 mixing only (50-500 L systems only).**

5.1 S.U.B.s require drive shafts and BPCs that are specifically made for low-volume mixing. For 50-500 L systems, the motor mount, drive shaft, and BPC should be engraved or labeled with "5:1 Mixing" and/or a warning tag. If any of these components are not labeled for 5:1 use, contact your sales representative immediately for a replacement.

5.2.2. Cell culture operation issues

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

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

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

Issue: Dissolved oxygen readings are erratic or unstable.

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

- Many different parameters can affect the ability of a bioreactor controller to maintain a target setpoint during process control. Modern controllers utilize computer algorithms to adjust targeted parameters; the most common technique is that of a tunable controller that uses variables of the 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. We recommend that you consult the user guide of the particular bioreactor controller you are using.
- A grounding reference to the media can be created by using a grounding lead between the tank and the body of the stainless steel DO probe or to the stainless steel connector (if present) on the sample line of the BPC.

Issue: pH levels are questionable or out of range.

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

- pH levels can be managed in a similar manner to conventional bioreactors once calibration of the probe is verified by use of an off-line sample. Carbon dioxide gas sparged through the media or headspace, biocarbonate levels in the media and the addition of liquid titrant solutions all serve to manage the pH balance of the bioreactor environment. See section 3.5.4 for more information on probe calibration.

- A grounding reference to the media can be created by using a grounding lead between the tank and the body of the stainless steel DO probe or to the stainless steel connector (if present) on the sample line of the BPC.

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

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

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

5.2.3. Sparging issues

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

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

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

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

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

- If the S.U.B. is filled with liquid and allowed to sit idle for extended periods of time without gas being supplied to the sparger, liquid can accumulate between the membrane and check valve. Various media additives may restrict the membrane temporarily. Several minutes of gas pressure being supplied to the sparger should purge the membrane, allowing it to function properly.
- Certain operating conditions can create situations when the sparger membrane may become restricted due to insufficient line pressure from the bioreactor controller gas feed line. Increasing the flow rate to one liter per minute, or momentarily raising the pressure regulator outlet pressure to 0.34 bar (5 psi) may alleviate the problem. Alternatively, several seconds at this higher pressure will allow the membrane to purge pores that may be blocked due to the presence of accumulated liquid.

5.2.4. Probe and connector issues

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

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

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

5.2.5. Other issues

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

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

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

Issue: **There is excessive pressure in the condenser bag for my 2,000 L system.**

Solutions: **Check for kinks in the exhaust tubing between the S.U.B. and the condenser bag.**

- Ensure that the condenser components are properly installed on the condenser hardware.
- Inspect the tubing regularly for kinks, and monitor the pressure.

Check for liquid buildup in the condenser bag outlet tubing and/or the vent filter.

- Ensure that the chiller power is on, the auto-restart option on the chiller is activated, and the chiller setpoint and actual temperature is correct.
- Ensure that the TCU coolant level in the chiller is at the maximum capacity before use, as low levels of coolant will increase the chiller plate temperature. **Note:** An infrared temperature reader can be used to confirm that the chiller plates are near the TCU setpoint (typically +/- 2°C of the setpoint).
- Check that the batch flow rates do not exceed recommendations.
- Check coolant lines between the chiller and condenser plate for abnormalities.
- Temporarily plug off vent filters (one at a time) while manipulating the tubing to drain liquids back into the condenser bag.
- Continuously monitor the pressure in the S.U.B.

Check the exhaust tubing between the S.U.B. and the condenser bag to ensure it is positioned correctly.

The braided exhaust hose tubing should not allow condensate to collect, but should be able to drain into the vessel or condenser.

Check for liquid buildup in the condenser bag.

- Ensure that the pump power is on, the auto-restart option on the pump is activated, and pump head is turning at the set speed, and the pump is set to recommended speed (12–30 rpm).
- Ensure that the pump tubing is properly installed in the pump head, and that there are no kinks or blockages in the liquid drain line tubing.

Ensure that foam has not reached the condenser bag. If the foam has reached the bag, reduce gas flow rates and add an anti-foam agent. After the foam has been controlled, it will naturally dissipate and drain out of the condenser bag.

Issue: **There is excessive residue buildup in the condenser bag for my 2,000 L system.**

Solution: **Ensure that the TCU coolant level in the chiller is always at maximum capacity before use.** Low levels of coolant will increase the chiller plate temperature, which results in excessive pressure and residue buildup in the bag. **Note:** An infrared temperature reader can be used to confirm that the chiller plates are near the TCU setpoint (typically +/- 2°C of the setpoint).

6

General ordering information

Chapter contents

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

6.1. Ordering instructions

BPCs and hardware components for the 5.1 Single-Use Bioreactor (S.U.B.) can be ordered directly from Thermo Fisher Scientific. These items include all components that have part numbers beginning with the following digits:

- SH
- SV
- SUB

6.2. Ordering/support contact information

In the Americas and Asia

1726 Hyclone Drive

Logan, Utah 84321

United States

Tel: +1 435 792 8500

Email: customerservice.bioprocessing@thermofisher.com

In Europe

Unit 9 Atley Way

Cramlington, NE 23 1WA

Great Britain

Tel: +44 (1) 670 734 093

Fax: +44 (1) 670 732 537

Email: customerservice.bioprocessing@thermofisher.com

6.3. Technical support

Technical support for the 5.1 S.U.B. is available in a variety of formats. Some or all of the following may be appropriate, depending on individual experience and circumstances.

Technical service hotline and email

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

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

Training

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

Appendix A—Installation of female electrical receptacle 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 control panel (E-Box) be modified to accommodate the cutout dimensions as shown in Figure A.1 below.
2. Verify that electrical power has been disconnected and locked out for safety.
3. Verify that the holes for mounting the receptacle housing are positioned properly. Center to center measurement of respective mounting holes is 85 mm (3.35 in.) tall and 77 mm (3 in.) wide.
4. Verify the condition of the three exposed wire leads and strip back to expose new wire if needed.

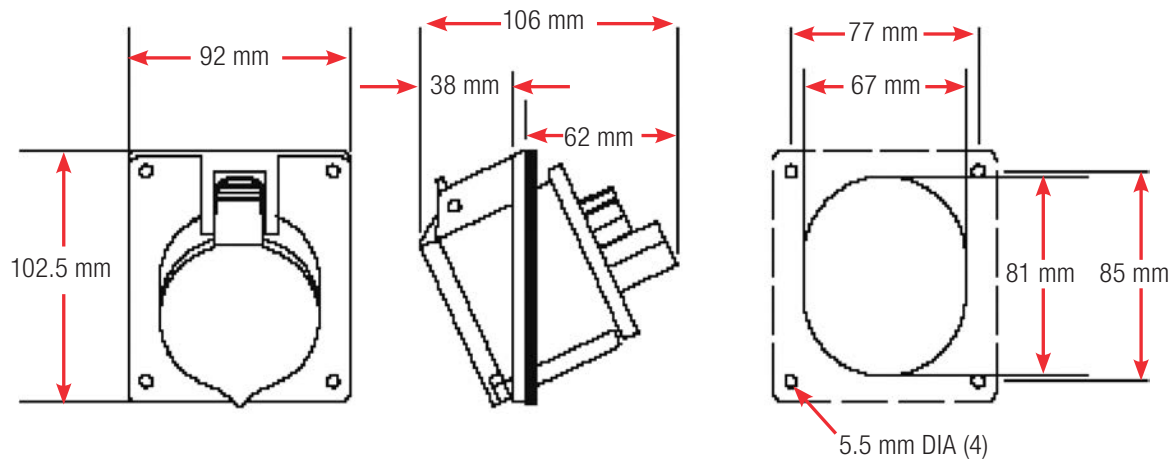


Figure A.1. Panel cutout.

5. Connect the wire leads on the receptacle (shown in Figure A.2 below) using the screw terminals, paying strict attention to obtain the correct wiring position as it is labeled on the receptacle.
 - Green (ground)
 - White (common)
 - Black in the U.S., Blue in the E.U. (hot)
6. If you are using the adapter mounting plate, secure it to the selected facility electrical housing as per drawing (Figure A.3 below), otherwise proceed to Step 7.

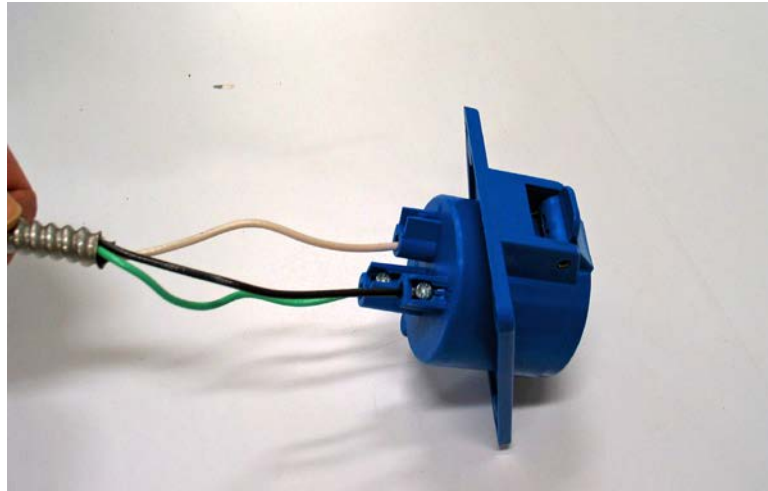


Figure A.2. Female receptacle (blue for 240 VAC, yellow for 110 VAC).

7. Secure the electrical receptacle using the 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.

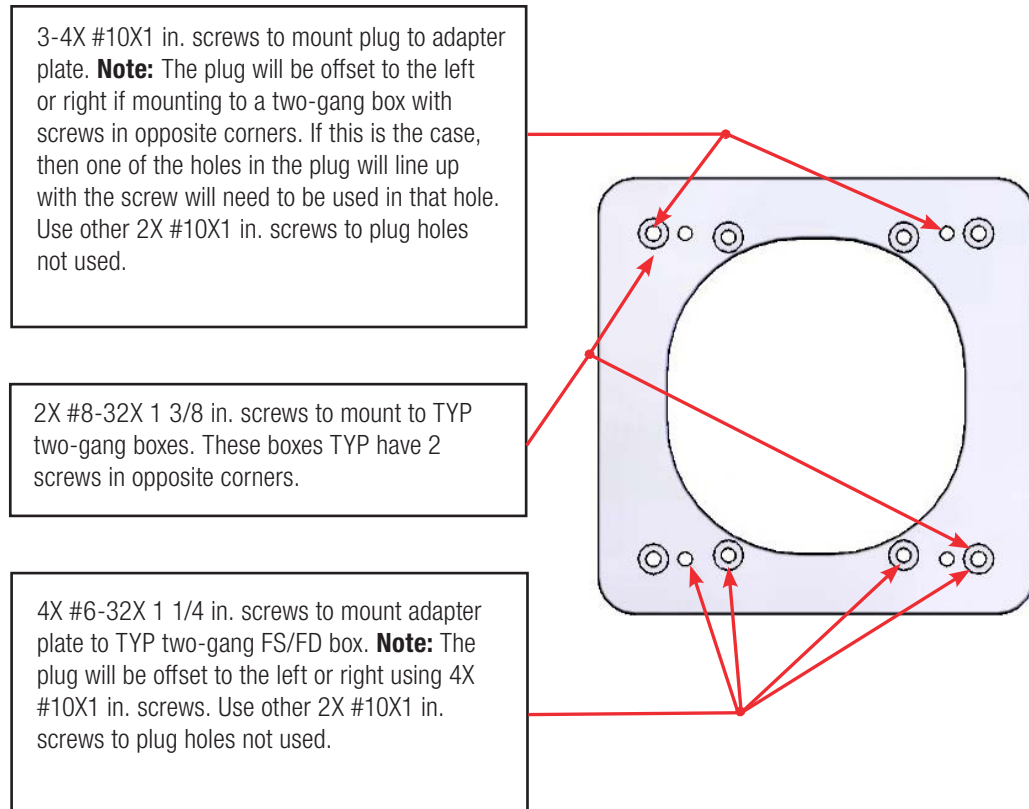


Figure A.3. Adapter mounting plate.

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 (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.B. electrical schematic contains a table showing the sub-blocks that have changed from the default settings.

Span calibration

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

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

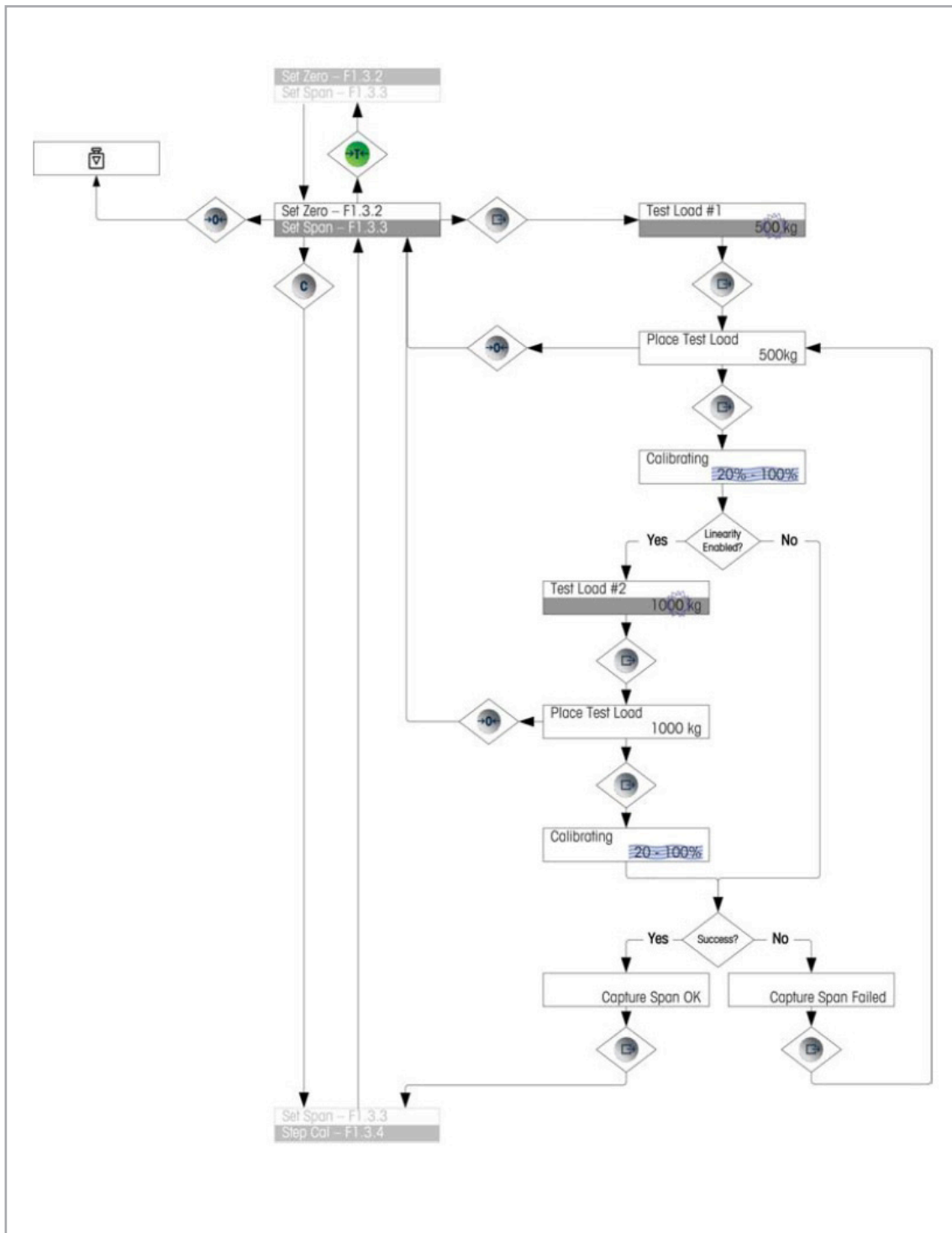


Figure B.1. Span calibration.

Appendix C—2,000 L S.U.B. agitator operation and maintenance guidelines

2,000 L Critical operating recommendations



WARNING: To prevent drive shaft breakage and maintain the equipment warranty, follow the operating recommendations listed below.

- ✓ Verify that the motor variable frequency drive (VFD) is programmed to accelerate and decelerate in a minimum of 60 seconds.
- ✓ Use a controller agitation speed governor and safety interlocks to prevent the system from running outside of recommended limits.
- ✓ Verify that the drive shaft serial numbers match on all segments; do not interchange shaft segments.
- ✓ Always maintain a log history of drive shaft usage (see Appendix D) and confirm that it has sufficient life remaining. If the age or history of a shaft is questionable, it should be replaced. For more information, see Maintenance in section 5.1 of this publication.
- ✓ Only activate agitation after the BPC has been filled with media.
- ✓ Use at least three operators to load the BPC into the 2,000 L S.U.B.
- ✓ Fully inflate the BPC prior to insertion of the drive shaft. This will keep the impeller tubing from stretching and being damaged.

Agitation speed recommendations

Table 3.3 in section 3.6.4 of this guide provides agitation speed recommendations for all system sizes. 2,000 L bioreactor recommendations are for systems with four-piece drive shafts, but two-piece shafts will provide equivalent or greater longevity.

Note: The nominal agitation recommendations in Table 3.3 are based on P/V values of 20 W/m^3 . This is the suggested default parameter for CHO cultivation. For more information on P/V calculation, see section 3.6.5 of this user's guide.

Find out more at thermofisher.com/sub

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