

# Xcellerex XDUO 2500 Mixer

## SINGLE-USE MIXING SYSTEMS

Achieve robust single-use mixing up to 2500 L throughout the entire process workflow with the versatile and easy-to-use Xcellerex™ XDUO 2500 (Fig 1). Perform fast and efficient mixing in upstream applications such as cell culture medium preparation and harvest using this large-volume mixer with exceptional mixing capabilities. Simplify complex and sensitive downstream mixing operations used in purification and separation processes with intelligent automation and process control. Support large-scale fermentors and bioreactors with these efficient and reliable mixers to fully realize the advantages of single use. This is made possible by a robust design and novel dual impellers mounted inside the disposable bag that can be jointly or independently controlled.

- Eliminate the need for complicated mating of motor and drive systems to storage tanks with the dual impellers and integrated magnetically coupled drives that enable faster setup and mixing times.
- Handle mixer bags easily and install them accurately with ergonomic and intuitive mixer and bag design.
- Achieve higher accuracy and consistency compared with manual methods through automation of pH and temperature.
- Eliminate the need to take multiple samples manually and minimize contamination risks with integrated in-line sensors.
- Monitor, trend, record, export, and print using advanced data management. 21 CFR Part 11 compliance-enabled.
- Minimize manual intervention by controlled locally or via FlexFactory™ Automation.



Fig 1. Three views of XDUO 2500 Mixer.

# Wide range of applications

## Upstream fed-batch applications

- Cell culture medium preparation
- Cell harvesting
- Intermediate product storage and pooling

## Upstream perfusion application

- Culture medium preparation for 200 L bioreactor, 1 to 2 medium volumes per day up to 10 d

## Downstream applications

- Buffer preparation: ultrafiltration/diafiltration (UF/DF)
- pH adjustment
- Viral inactivation
- Dilution
- Chromatography pooling
- Homogenization of protein solutions
- Homogenization of vaccine adjuvants
- Intermediate storage and pooling

## Application advantages

The range of in-process monitoring and control capabilities of the XDUO 2500 allows precise configuration for a wide range of application needs—reducing your capital equipment requirements and maximizing your plant efficiency.

**Automated viral inactivation** with in-line sensors, programmable logic control (PLC), and pumps saves time and minimizes errors.

**Automated pH adjustment** enables equilibration of cell culture medium and buffer preparation, without sampling or manual addition of titrants.

**Formulation** in the closed system provides processing with minimized contamination risk.

## Bag assembly

XDUO 2500 delivers flexibility with the availability of two bag types: Standard and Plus. The bags include varying numbers of tubing lines and connections as well as sampling and sensing capabilities to accommodate a wide array of applications. Custom bag configurations are also available on request. The bag has two disposable high-strength impellers welded to the bottom of the bag assembly (Fig 2). Features of the bag and rigid container also permit seamless transitioning between solid-liquid and liquid-liquid mixing applications. The engagement between motor and disposable impeller is via a robust magnetic coupling, imparting high torque and rapid mixing capability to the system. The disengagement between the motor and disposable impeller is via a decoupler mechanism, enabling secure and easy bag removal. Figure 3 shows a rendering of the bag assembly.



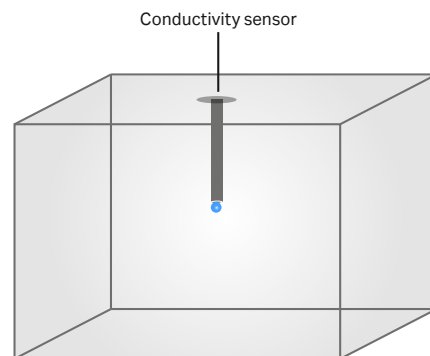
**Fig 2.** The disposable impeller is welded to the bottom of the bag.



**Fig 3.** The XDUO 2500 L bag with dual, bidirectional impellers.

## Mixing time study using conductivity tests

Different mixing studies were conducted to quantitate the mixing time benefits of using a dual impeller. Conductivity measurement was used to understand the mixing time and the sensor was placed in the central position shown in Figure 4. The center probe is critical for conductivity measurement because it is located away from the impellers and walls and is an excellent indicator of mixing efficiency.



**Fig 4.** Conductivity probe placement, liquid-liquid and solid-liquid mixing studies.

## Liquid-liquid mixing study

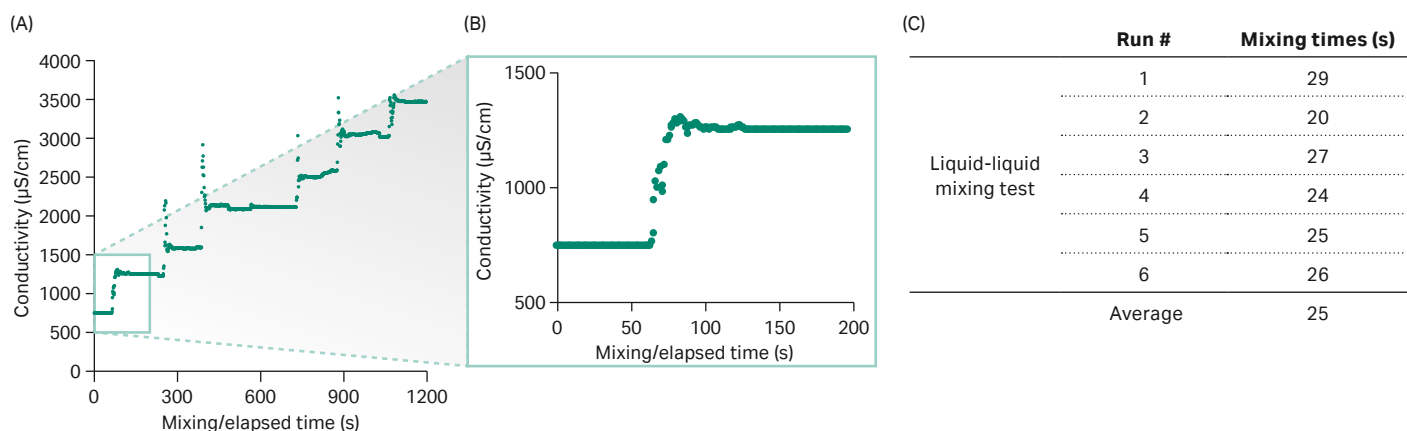
In evaluation, six runs were conducted, each consisting of the addition of 5 L of a 2 M NaCl solution in water. Two ranges of conductivity and mixing speed were evaluated. Figure 5A shows mixing results at 700 to 3500  $\mu\text{S}/\text{cm}$  conductivity and 300 rpm (clockwise downpumping). The results show consistent mixing results for all additions of NaCl solution.

## Solid-liquid mixing study

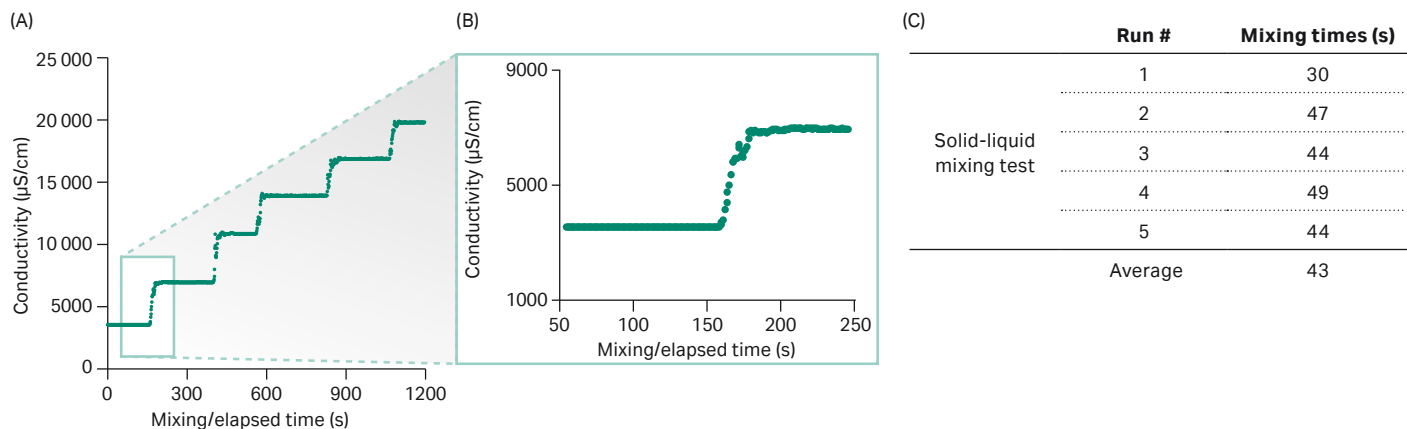
In evaluation, five runs were conducted, each consisting of the addition of 5 kg of USP grade NaCl in water. Figure 6A shows results of the mixing at 3000 to 20 000  $\mu\text{S}/\text{cm}$  conductivity at 300 rpm (clockwise downpumping). Consistent mixing of solid 5 kg of NaCl was observed for each run.

## Heating-cooling performance using temperature mapping

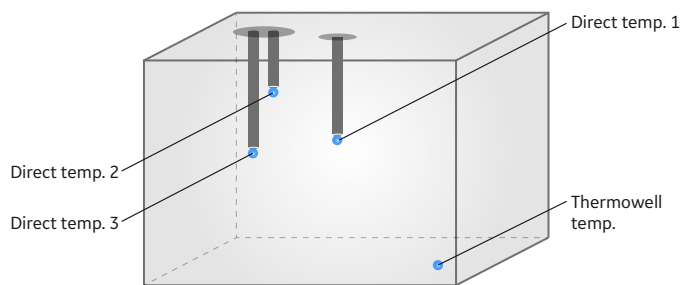
Heating and cooling performance of the five-face jacket (bottom and four sides) was tested with 2500 L water in the mixer. The probe placement at different points for temperature measurements taken in the study is shown in Figure 7. Temperature control unit (TCU) heat transfer fluid was composed of 20% propylene glycol/80% water. The TCU specifically designed for this mixer has 9 kW of heating power and  $\sim 54 \text{ MJ/h}$  ( $\sim 51 \text{ 180 BTU/h}$ , 15 kW) of cooling power.



**Fig 5.** Liquid-liquid mixing study. Six runs were conducted, each consisting of the addition of 5 L of a 2 M NaCl solution to water. Conductivity was measured at 300 rpm mixing speeds.



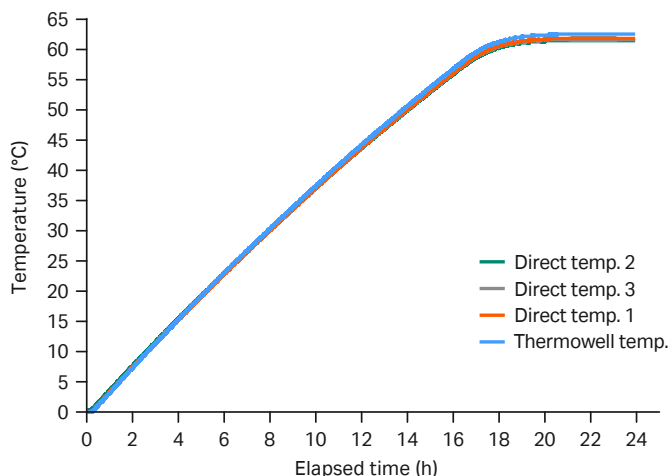
**Fig 6.** Solid-liquid mixing. Five runs were conducted, each consisting of the addition of 5 kg of USP grade NaCl in water. Conductivity was measured at 300 rpm mixing speeds.



**Fig 7.** Resistance temperature detector (RTD) probe placement for thermal performance study.

The heating test was conducted with a single step ramp-up profile from 2°C to 60°C (TCU set point: 65°C). The cooling test was conducted with single step ramp-down profile from 60°C to 2°C (TCU set point: -2°C).

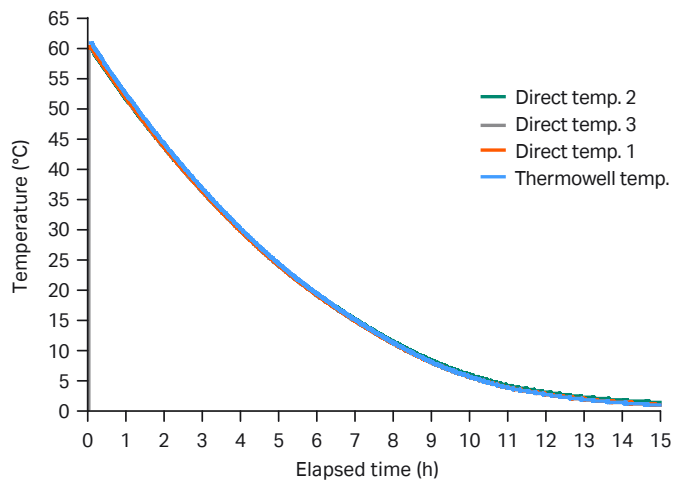
Effective heating and cooling performance of 2500 L of water was observed in the study. The results are shown in Figures 8 and 9, respectively, and summarized in Tables 1 and 2. Intermediate heating and cooling performance were derived from the data and are also shown in the figures.



**Fig 8.** Heating of 2500 L of water in XDuo 2500 Mixer from 2°C to 60°C in 17 h. The curves show measurements made at four separate points in the mixing chamber.

**Table 1.** Heating of 2500 L of water in XDuo 2500

Temp range (°C)	Elapsed time (h)	Average change in direct temp (°C)	Heating rate (°C/h)
2 to 60	0.61 to 17.00	57.41	3.50
2 to 20	0.61 to 5.00	17.50	3.99
20 to 60	5.00 to 17.00	39.91	3.33



**Fig 9.** Cooling of 2500 L of water in XDuo 2500 from 60°C to 2°C in 12 h. The curves show measurements made at four separate points in the mixing chamber.

**Table 2.** Cooling of 2500 L of water in XDuo 2500




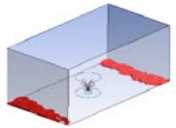
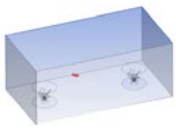



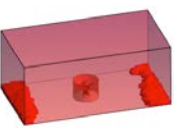
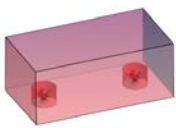
Temp range (°C)	Elapsed time (h)	Average change in direct temp (°C)	Cooling rate (°C/h)
60 to 2	0.00 to 12.00	-58.04	4.84
60 to 4	0.00 to 11.00	-56.94	5.18
60 to 20	0.00 to 6.00	-41.50	6.92
20 to 2	6.00 to 12.00	-16.54	2.76

## Effect of tank shape and impeller quantity on salt settling and dispersion

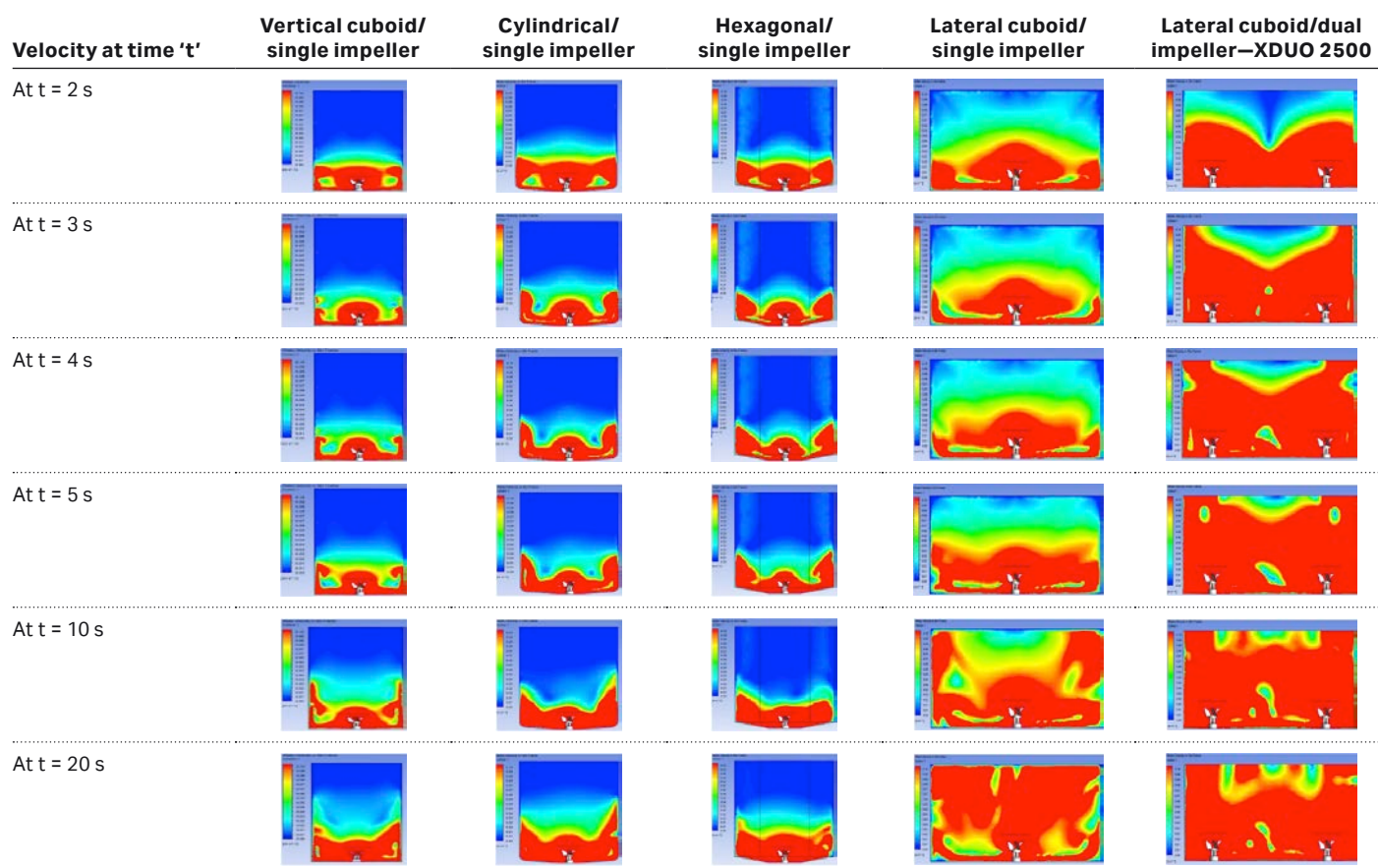
Tank shape, impeller design, and impeller location was evaluated for a range of mixer designs, including the XDuo 2500. Salt settling and dispersion phenomena were used to evaluate the mixing performance.

The settling study plots in Figure 10 show the location and quantity of settled particles (shown in red) in different tank shapes. Minimal particle settling (0.5%) was observed in XDuo 2500. The dispersion study plots in Figure 10 show excellent distribution of particles throughout the XDuo 2500 (red area).

The velocity contour plots in Figure 11 show how quickly the momentum is transferred from the impeller and reaches the top of the tank. The red area in the plots shows mixing velocity of > 0.1 m/s. The results clearly demonstrate how quickly the momentum is transferred from the impeller to reach the top of the tank. In conclusion, the lateral, cuboid design of the XDuo 2500 combined with the dual impellers allows rapid efficient mixing, right to the top of the tank in as little as 4 s.

Study type	Vertical cuboid/ single impeller	Cylindrical/ single impeller	Hexagonal/ single impeller	Lateral cuboid/ single impeller	Lateral cuboid/dual impeller—XDUO 2500
Settling study	 5.8 kg or 30.5%	 0.0 kg or 0.0%	 5.5 kg or 28.9%	 16 kg or 84.2%	 0.1 kg or 0.5%
Dispersion study	 1266 L or 50.8%	 1200 L or 48%	 1075 L or 43%	 2500 L or 100%	 2500 L or 100%

**Fig 10.** Settling and dispersion characterization in different tank shapes.



**Fig 11.** Momentum transfer characterization in different tank shapes. Velocity contours (red = 0.1 m/s and above, blue = stagnant region).

## Cytiva's range of single-use mixers

Xcellerex single-use mixers are available as XDM and XDUO configurations and in a range of sizes to cover many bioprocessing applications. In terms of mixing capability, the XDM and XDUO are identical. XDUO, however, offers more powerful automation capabilities. The XDM mixers range in size from 50 to 1000 L, while XDUO mixers are available from

100 to 2500 L. In common for all configurations is the robust mixing performance and ease of use. The mixers are designed for process development, commercial and clinical production of biopharmaceuticals, vaccines, and other biologics. Xcellerex mixers support upstream and downstream applications for preparation of buffer, media, product and intermediates, as well as other process fluids.



# Specifications

Vessel and system specifications are listed in Table 3, and site preparation guide is shown in Table 4.

**Table 3.** Vessel and system specifications<sup>1</sup>

For hardware ordering, contact your Cytiva sales representative.

## Vessel

Vessel interior (W × H × D)	2083 × 1054 × 1118 mm (82 × 41.5 × 44 in)
Vessel overall dimensions with I/O panel (W × H × D)	2591 × 1605 × 1260 mm (102 × 63 × 49.6 in)
Geometry	Cuboid with sloped bottom for full drainability
Vessel main construction material	304 SS ASTM material
Vessel surface finish	Ra ≤ 35 µin, ≤ 1.0 µm
Slope to drain	1.54°, 0.27 mm/meter
Mobility (casters)	Mounted on four clean room casters and push handles
Caster dimensions (ø × W)	90 × 55, max. load 2000 kg /each
Weight (empty)	1200 kg (2645 lb)
Bag tubing gate	Side port (long face) for bag lines and sensor access
Easy bag access	Two side ports (short face) for bag handling

## Jacket

Jacket type	Four sides and bottom-dimple style
Insulation type	Four sides, bottom, and lids on top
Jacket volume	39.5 L
Jacket (design working pressure/test pressure)	0.69/0.88 MPa, 6.9/8.8 bar, 100/130 psig
Burst disk rating	0.25 MPa, 5.2 bar, 75 psig
Compliance	ASME pressure vessel code compliant
Heat transfer fluid I/O connections	25.4 mm (1 in) SCH 40 pipe with male NPT thread
Drain ports	Qty 2: 12.7 mm (0.5 in) SCH 40 pipe with male NPT thread, Qty 1: 25.4 mm (1 in) SCH 40 pipe with male NPT thread (shared inlet)

## Agitation

Motor – quantity/type	2 × Siemens SIMOGEAR™ Bevel Geared AC Motor
Motor – mounting	Bottom integrated with vessel
Motor – power (rating)/requirement	0.75 HP (550 W)/230 V (60 Hz)
Motor drive – type	Dual drive – independent variable frequency control
Motor drive – functionality	Run/stop, forward/reverse, 10 to 300 rpm

## Ingress protection

Motor	IP 67
I/O panel	IP 55
Field-mounted instrumentation, sensors	≥ IP 54

## Smart control unit

Control panel	Integrated dual cabinet – high and low voltage
Dimensions (W × H × D)	460 × 422 × 279 mm (18.1 × 16.6 × 11 in) (enclosure only, not including parts mounted on external surfaces)
Constructions material and surface finish	304 SS ASTM, surface finish: Ra ≤ 35 µin, ≤ 1.0 µm
Automation hardware	Siemens SIMATIC™ S7-1200 PLC
Automatic pH control pump	Watson-Marlow™ LF peristaltic pump, 520VBM, 190 rpm
Automatic pH control Transmitter	Rosemount™ Analytical Model 1056 Dual Input Analyzer
Automatic temperature control	Jacketed tank and external temperature control unit (optional)
HMI	Siemens SIMATIC 7 in—HMI comfort panel—touch screen color
Alarms	Factory set and user defined
Communication ports	USB, Ethernet, PROFIBUS™
Remote connectivity	FlexFactory using M-Station. Other biomanufacturing platforms using X-Station.
E-stop	Integrated safety circuit for entire system
Automation compliance	Built to EU Annex 11 regulations, GAMP™ 5 guidelines

## Process analytics

Data monitoring	Real-time instantaneous and trending of all variables
Data recording	Long-term data recording of all variables
Data storage	HMI SD card
File formats	CSV
Data security	Two-level protection
Data printing	Enabled
Data exporting	Local via USB Flash drive. Remote via PC (with Ethernet and web browser capabilities)
Audit log	21 CFR Part 11 enabled

## Integrated process monitoring

RTD temperature sensor	Burns Eng., model 22041-07010
Ph Probe	Hamilton™ EasyFerm™ Plus VP 225, P/N 238634/00
Conductivity probe	Hamilton Conducell™ 4USF-PG-120, P/N 23899-4047/99
Load cells	Mettler Toledo 0745A
Summing box	Mettler Toledo Summing Box (61005973)
Sensor installation time	< 30 min

## Recommended operating conditions

Ambient operating temperature	5°C to 30°C
Jacketed operating temperature	2°C to 60°C
Motor speed	10 to 300 rpm
Absolute min. volume	520 L
Absolute max. volume	2600 L
Maximum closed-top mixing bag pressure	0.005 MPa (0.05 bar, 0.7 psig)
Continuous operating time	5 d (for bag)
Relative humidity	20% to 95%, noncondensing min imum
Cleaning agents	External surfaces of the system components are compatible with commonly used cleaning methods in GMP and lab environments

<sup>1</sup> All specifications are subject to change without notice.

**Table 4.** Site preparation guide**1. Containers**

Dimensions (W × H × D)	
XDUO 2500 jacketed	168 × 219 × 293 cm (66 × 86 × 115 in)
XDUO 2500 nonjacketed	168 × 219 × 293 cm (66 × 86 × 115 in)
Step ladders (optional)	92 × 74 × 102 cm (36.1 × 29.1 × 40.1 in)
Total crate and unit weights	
XDUO 2500 jacketed	1742 kg (3840 lb)
XDUO 2500 nonjacketed	1470 kg (3241 lb)
Step ladders (optional)	68 kg (150 lb)

**2. Uncrating the system**

Tools required	Forklift or pallet jack
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**3. Power requirements**

I/O cabinet supply voltage	100 to 120 V AC, 50 or 60 Hz, 12 A 220 to 240 V AC, 50 or 60 Hz, 6 A
Unit maximum power consumption	1.8 kVA

## Single-use bags

Specifications of the single-use bags are listed in Table 5. The Xcellerex bag assembly connections for use with XDUO 2500 are described in Table 6 and in Figure 12.

**Table 5.** Single-use bag specifications<sup>1</sup>

Dimensions (W × H × D)	2083 × 1092 × 1143 mm (82 × 43 × 45 in)
Maximum volume	2600 L
Nominal volume	2500 L
Minimal (for mixing)	520 L
Hold-up volume	2.5 L
Fluid contact layer (film material)	Low-density polyethylene
Pressure rating (max. operating)	0.005 MPa, 0.05 bar, 0.70 psig
Sterilization	Dosed at 27.5 to 45 kGy
Product recovery	> 99.9%
Bag setup time	< 10 min for one person < 5 min for two persons

**Impeller specifications**

Impeller position	Symmetric
Impeller	Two impellers (four blades each)
Impeller material	HDPE (natural)
Tubing material	C-Flex® 374 or Advantaflex™

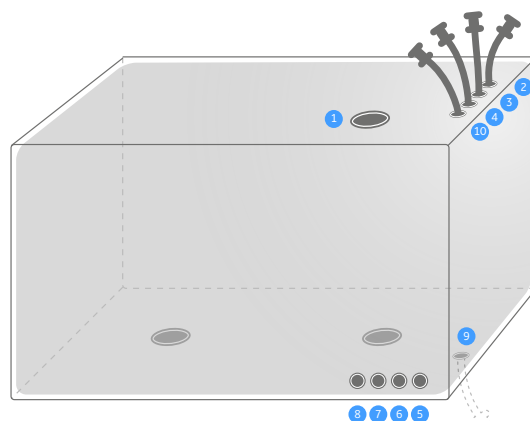
<sup>1</sup> All specifications are subject to change without notice.

**Table 6.** Xcellerex single-use bag assembly connections<sup>1</sup>

Port description		Fortem bag assembly	Fortem plus bag assembly
1	Fill port: 3 in (76.2 mm) Tri-Clamp™ powder addition port, capped	x	x
2	AdvantaFlex tubing, 4 ft (121.9 cm) with plugged end	–	6.35 mm (1/4 in)
3	AdvantaFlex tubing, 4 ft (121.9 cm) with plugged end	–	6.35 mm (1/4 in)
4	AdvantaFlex tubing, 4 ft (121.9 cm) with clamp, plugged, ReadyMate™ DAC, or Aseptiquik™ G	25.4 mm (1 in)	25.4 mm (1 in)
5	Sample line: AdvantaFlex tubing, 18 in (45.7 cm) with clamp and swabable valve connection	3.18 mm (1/8 in)	3.18 mm (1/8 in)
6	Thermowell: for noninvasive temperature sensing	–	x
7, 8	Probe port: Aseptiquik G connector port for probe connection	–	x
9	Harvest/drain: AdvantaFlex tubing, 4 ft (121.9 cm) with clamp, plugged, ReadyMate DAC, or Aseptiquik G	25.4 mm (1 in)	25.4 mm (1 in)

Port description		Standard bag assembly	Plus bag assembly
1	Fill port: 3 in (76.2 mm) Tri-Clamp™ powder addition port, capped	x	x
2	C-Flex 374 tubing, 4 ft (121.9 cm) with ReadyMate DAC	–	6.35 mm (1/4 in)
3	C-Flex 374 tubing, 4 ft (121.9 cm) with ReadyMate DAC	–	12.7 mm (1/2 in)
4	C-Flex 374 tubing, 4 ft (121.9 cm) with clamp and ReadyMate DAC	25.4 mm (1 in)	25.4 mm (1 in)
5	Sample line: 18 in (45.7 cm) C-Flex 374 tubing with clamp and Luer connection	3.18 mm (1/8 in)	3.18 mm (1/8 in)
6	Thermowell: for noninvasive temperature sensing	–	x
7, 8	Probe port: female Kleenpak™ Connector port for probe connection	–	x
9	Harvest/drain: C-Flex 374 tubing, 4 ft (121.9 cm) with ReadyMate DAC	25.4 mm (1 in)	25.4 mm (1 in)
10	C-Flex 374 tubing, 4 ft (121.9 cm) with ReadyMate DAC	–	6.35 mm (1/4 in)

<sup>1</sup> All specifications are subject to change without notice.

**Fig 12.** XDUO 2500 L bag configuration. Positions 1 to 10 are described in Table 6.

# Ordering information

Product	Product code
Xcellerex XDUO 2500 Mixer	29163525
Plus bag	888-0289-C
Standard bag	888-0857-C
Fortem bag	29302484
Fortem plus bag	29301053
Fortem bag with ReadyMate	29395008
Fortem plus bag with ReadyMate	29395009
Fortem bag with Aseptiquik	29395115
Fortem plus bag with Aseptiquik	29395116

Accessories	Product code
Lid XDM 2500	29206864
Lid XDM 2500 (2)	29206865
Drain plate XDM 2500	29206866
Probe bracket assembly	29206867
Port hole cover assembly (metric)	29206868
Clamp 1 in 13 MHHM XDMT	29206869
XDUO 2500 hose kit	29206872
XDM hopper	817-00091
Insert pH, 12 × 225 mm, Hamilton, VP	817-00144
Insert conductivity, 12 × 225 mm	817-80003
Reusable probe stand autoclave	826-00304
Assure probe sheath (4)	29207815
Probe sheath (4)	888-0138
XDM 2500 Plus Quad MBA	888-0289-C
Probe clamp plier	888-0341
5 kg Fortem film powder bag	29399774
10 kg Fortem film powder bag	29399775
10 kg powder bag	888-0358
5 kg powder bag	888-0375

Related literature	Product code
Automated pH adjustment on an intelligent, single-use mixing platform, application note	29091383
Using Xcellerex mixing system as a slurry tank when packing chromatography columns, application note	29056440
Heating/cooling and liquid/liquid mixing characterization at a range of volumes in Xcellerex XDM and XDUO single-use mixers, poster	29207530
Xcellerex XDUO Mixer, datafile	29048366
Xcellerex XDM Mixer, datafile	29048367
Xcellerex XDR cell culture bioreactor systems, datafile	29092925

For more information on the mixing systems, please contact your local sales representative.

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