Xcellerex XDUO Mixer

SINGLE-USE MIXING SYSTEMS

Xcellerex™ XDUO Mixer is a single-use mixing system for clinical and commercial production of biopharmaceuticals, vaccines, and other biologics (Fig 1). Use this intelligent, plug-and-play system in upstream and downstream applications for automated mixing of buffer, media, product and intermediates, as well as other process fluids. Achieve robust mixing and ease of use with XDUO, which features powerful onboard automation capabilities, including in-line sensing, load cells, and process control. XDUO integrates with existing biomanufacturing production lines as well as with the FlexFactory™ biomanufacturing platform.

- Reduce downtime and costs that would otherwise be needed for cleaning and cleaning validation procedures.
- Achieve quick start-up of unit operations and mixing processes via the onboard instrument panel.
- View live process data and trends that are automatically displayed on the instrument panel.
- Control XDUO locally, or via FlexFactory automation to minimize manual intervention.
- Achieve greater accuracy and significant time savings with automated titration.
- Eliminate the need for manual logging, as XDUO logs process data and events for input into batch records.

Application advantages

The range of in-process monitoring and control capabilities of the XDUO allows precise configuration for a wide range of application needs. This flexibility reduces capital equipment requirements and maximizes plant efficiency.

Fig 1. Xcellerex XDUO Mixer is available in sizes of 100, 200, 500, 1000, and 2500 L in either stainless steel or jacketed stainless steel (for heating and cooling applications). XDUO-2500L is described separately in data file 29153543.

- **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 media and buffer preparation, without sampling or manual addition of titrants.
- **Formulation** in the closed system provides processing with reduced risk of contamination.

Recommended applications include:

- Medium preparation
- Buffer preparation
- pH adjustment
- Resuspension
- Chromatography pooling
- Homogenization of protein solutions
- Homogenization of vaccine adjuvants
- Viral inactivation
- Intermediate storage and pooling
- Ultrafiltration/diafiltration (UF/DF)
- Final formulation
- Cell harvest

Onboard capabilities:

- Data trending and recording
- Remote operation interface with FlexFactory automation
- Configurable with either dual pH monitoring, or single pH and conductivity monitoring
- pH control
- Temperature monitoring and control
- Weight monitoring

Bag assembly details

Two bag types (Standard and Plus) are available for XDUO single-use mixers. Both bag types have tubing lines and connections, as well as sampling and sensing capabilities to accommodate a wide array of applications. Alternate versions of these bags are available to optimize their use with different equipment, including plugged ended and unique sterile connector configurations. Custom bag configurations and filtration assemblies are also available on request. Features of the bag and rigid container permit seamless transitioning between powder-liquid and liquid-liquid mixing applications. A disposable impeller is welded into the bottom of the bag assembly (Fig 2). The engagement between motor and disposable impeller is via a robust magnetic coupling, imparting high torque and rapid mixing capability to the system.

Fig 2. The disposable impeller assembly is welded to the bottom of the bag for robust and reliable performance.

Single-use mixer product range

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. All configurations provide robust mixing performance and ease of use. The mixers are designed for process development, clinical and commercial 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.

Thermal and mixing characterization

In a typical biopharmaceutical plant, a substantial amount of time is spent on mixing or hydration. A mixing vessel is required for operations spanning preparation of cell culture media and buffers to mixing of product in the intermediate storage steps and even during viral inactivation. Single-use mixers have been used in the past two decades in biopharmaceutical plants to replace the use of stainless steel vessels. XDM and XDUO mixers from Cytiva offer equivalent mixing capabilities, with XDUO exhibiting a higher level of automation. Heating-cooling and mixing properties are the two key parameters important for mixing applications. Information about these properties is needed when comparing the performance between stainless steel and single-use mixers.

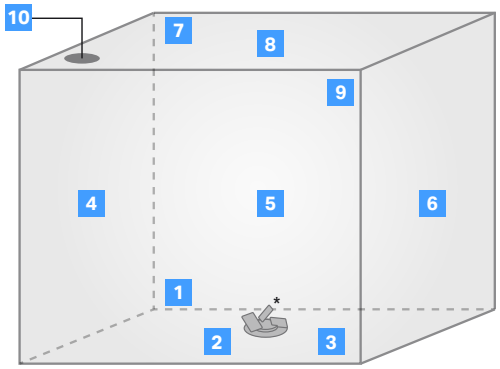
Two parameters—heating-cooling time and liquid-liquid mixing time—were characterized for a range of volumes and impeller speeds in the XDM-50L as well as in the XDM/XDUO-200L and 500L mixers.

Mixing time to 95% homogeneity (t_{m95}) was measured by acid pulse addition at nine different pH probe locations in the bags (Fig 3). Figure 4 shows heating-cooling times at maximum working volumes for the three different mixer sizes. Figure 5 displays mixing times measured at the different probe positions for the highest settings of volume and impeller speed. Contour plots describing the effect of impeller speeds, volumes, and viscosities on liquid-liquid mixing are shown in Figure 6.

The results show homogeneous mixing across all probe locations. Excellent comparability in terms of liquid-liquid mixing time and time to heat-cool the mixer content was observed for all mixer sizes tested.

Table 1. The heating-cooling and liquid-liquid test conditions

Parameters	Settings: heating-cooling	Settings: liquid-liquid mixing
Liquid volumes (min, mid., max. [L])	17, 33.5, 50 (XDM-50L)	
	44, 122, 200 (XDUO-200L)	
	110, 305, 500 (XDUO-500L)	
Temperature intervals, heating	5°C to 20°C, 20°C to 37°C	20°C
Temperature intervals, cooling	37°C to 20°C, 20°C to 5°C	N/A
Impeller speed	125 rpm	50, 75, 125, 175, 200 rpm
Impeller direction	Up flow	Up flow
Liquid	0.1 M NaCl (aq.) solution	0.1 M NaCl (aq.), sucrose for viscosity, 0.2 M HCl/0.2 M NaOH for pH shifts



1 Bottom corner, opposite standard position (3)
2 Bottom between impeller and wall
3 Standard pH probe location, standard position
4 Middle of wall
5 Middle of tank
6 Middle of wall
7 Top corner
8 Top of tank, centered
9 Top corner
10 Addition port

* The impeller assembly is welded to the bag. The impeller shown is for XDM/XDUO-100L, 200L, and 500L mixers; the equivalent impeller for XDM-50L is not shown.

Fig 3. Distribution of the nine pH probes (blue points) deployed in the mixing time characterization of XDM/XDUO mixers.

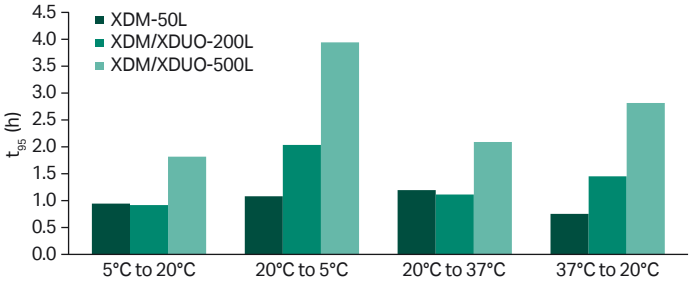


Fig 4. Heating and cooling times (t_{95}) for different temperature ranges. Measured at max. working volume for the 50, 200, and 500 L mixers.

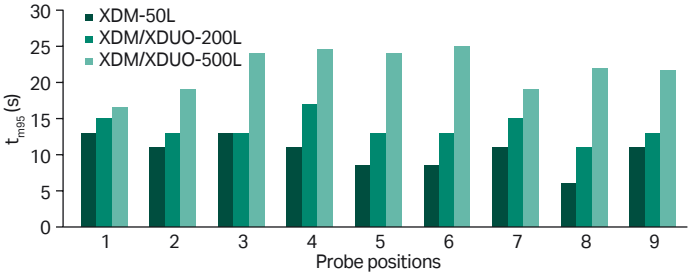


Fig 5. Liquid-liquid mixing time (t_{m95}) at each of the nine probe positions at maximum volume, 10 cP viscosity, and 175 rpm impeller speed.

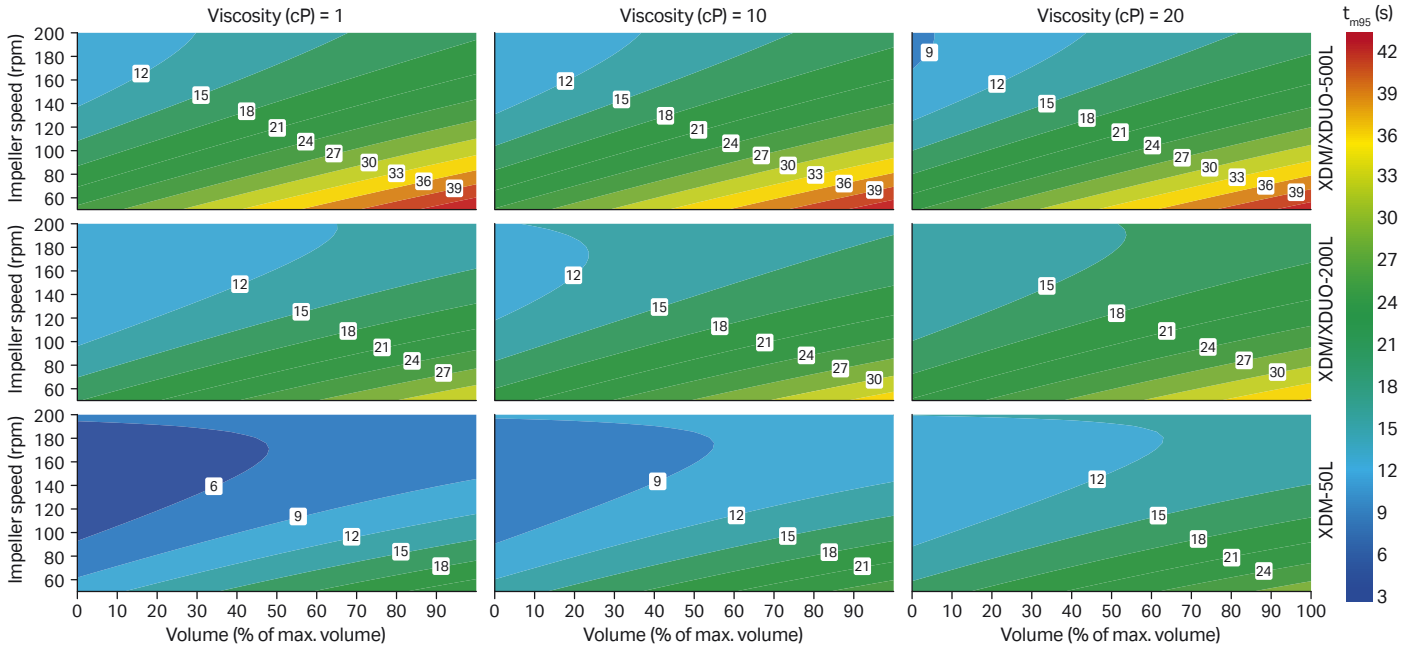


Fig 6. Contour plot showing mixing time (t_{m95}) in seconds of XDM-50L and XDM/XDUO-200L and 500L mixers under different settings (impeller speed, volume, and viscosity). The plot was generated from the probe positions resulting in the longest mixing time (t_{m95}) for each run.

Specifications

Vessel specifications are given in Table 2, and system specifications are listed in Table 3. Site preparation guide is shown in Table 4.

Table 2. Vessel specifications[1]

XDUO Jacketed Mixer	100 L	200 L	500 L	1000 L
Vessel				
Vessel interior dimensions (W × H × D)	508 × 498 × 508 mm (20 × 20 × 20 in)	635 × 636 × 635 mm (25 × 25 × 25 in)	838 × 851 × 838 mm (33 × 33 1/2 × 33 in)	1040 × 1023 × 1040 mm (41 × 38 × 41 in)
Vessel overall dimensions with I/O panel (W × H × D)	1010 × 1090 × 870 mm (39 7/8 × 43 × 34 1/4 in)	1140 × 1120 × 1000 mm (44 7/8 × 44 1/8 × 39 3/8 in)	1350 × 1480 × 1200 mm (53 1/4 × 58 3/8 × 47 1/4 in)	1550 × 1590 × 1410 mm (61 1/8 × 62 5/8 × 55 5/8 in)
Geometry	Cube with sloped bottom for full drainability			
Vessel main construction material	ASME II SA-240 304 L (stainless steel)			
Vessel surface finish	RA 0.8			
Slope to drain	2.5°			
Mobility (casters)	Mounted on four clean room casters and push handles			
Caster dimensions (ø × W)	100 × 35 mm	125 × 40 mm	125 × 40 mm	160 × 45 mm
Weight (empty)	155 kg (342 lb)	200 kg (441 lb)	315 kg (695 lb)	440 kg (970 lb)
Bag tubing gate			Side port (front face) for bag lines and sensor access	Side port (front face) for bag lines and sensor access
Easy bag access			One side port for bag handling	One side port for bag handling
Jacket				
Jacket type	Four sided dimple style			
Insulation type	PAROC Pro Wired Mat 70 or similar			
Jacket volume	3.8 L	4.0 L	8.0 L	9.0 L
Jacket (max. design working pressure/test pressure)	6.9 / 9.0 bar			
Burst disk rating	0.59 MPa, 5.9 bar, 85 psig			
Compliance	ASME sec VIII Div 1 - 2015			
Heat transfer fluid supply/return connections	Parker quick couplings 316 SS (FS-1002-16FP/FS-1001-16FP)			
Drain ports	Capped with ball valve			
XDUO Non-jacketed Mixer	**100 L**	**200 L**	**500 L**	**1000 L**
Vessel				
Vessel interior dimensions (W × H × D)	508 × 498 × 508 mm (20 × 20 × 20 in)	635 × 636 × 635 mm (25 × 25 × 25 in)	838 × 851 × 838 mm (33 × 33 1/2 × 33 in)	1040 × 1023 × 1040 mm (41 × 38 × 41 in)
Vessel overall dimensions with I/O panel (W × H × D)	910 × 1090 × 640 mm (35 7/8 × 43 × 25 1/4 in)	1030 × 1120 × 770 mm (40 5/8 × 44 1/8 × 30 3/8 in)	1240 × 1480 × 970 mm (48 7/8 × 58 3/8 × 38 1/4 in)	1440 × 1590 × 1180 mm (56 3/4 × 62 5/8 × 46 1/2 in)
Geometry	Cube with sloped bottom for full drainability			
Vessel main construction material	ASME II SA-240 304 L (stainless steel)			
Vessel surface finish	RA 0.8			
Slope to drain	2.5°			
Mobility (casters)	Mounted on four clean room casters and push handles			
Caster dimensions (ø × W)	100 × 35 mm	125 × 40 mm	125 × 40 mm	160 × 45 mm
Weight (empty)	115 kg (254 lb)	140 kg (309 lb)	200 kg (441 lb)	310 kg (684 lb)
Bag tubing gate	Side port (front face) for bag lines and sensor access			
Easy bag access	Two side ports (short face) for bag handling	Two side ports (short face) for bag handling	One side port for bag handling	One side port for bag handling

[1] All specifications are subject to change without notice.

Table 3. System specifications[1]

	100 L	200 L	500 L	1000 L
Agitation				
Motor quantity/type	1 × Groschopp™ AC motor (2414597-1013)			
Motor mounting	Bottom integrated with vessel			
Motor drive type	Variable frequency drive (Allen-Bradley™ PowerFlex™ 525)			
Motor drive functionality	Run/stop, forward/break/reverse, 10 to 200 rpm			
Ingress protection				
IP code	IP 45			
Smart control unit				
Control panel	Integrated cabinet			
Dimensions (W × H × D)	285 × 600 × 450 mm (11 × 24 × 18 in)	285 × 600 × 450 mm (11 × 24 × 18 in)	285 × 600 × 450 mm (11 × 24 × 18 in)	285 × 600 × 450 mm (11 × 24 × 18 in)
Constructions material and surface finish	ASME II SA-240 304 L (stainless steel); RA 0.8			
Automation hardware	Siemens™ S7-1200 PLC			
Automatic pH control pump	Watson-Marlow™ 313 OEM peristaltic pump			
Automatic pH control transmitter	Rosemount™ analytical model 1056 Dual Input Analyzer			
Automatic temperature control	Jacketed only: external temperature control unit optional			
HMI	Siemens SIMATIC™ HMI TP700			
Alarms	Factory set and user defined			
Communication ports	USB, Ethernet, Profibus			
Remote connectivity	FlexFactory using M-Station. Other biomanufacturing platforms using X-Station (custom)			
E-stop	Integrated safety circuit for pH pumps			
Automation compliance	21 CFR Part 11 and EU Annex 11 compliance enabled			
Process analytics				
Data monitoring	Real-time instantaneous and trending of all variable			
Data recording	Long-term data recording of all variable			
Data storage	HMI SD card			
File formats	CSV			
Data security	Three-level security (administrator, super-user and operator)			
Data exporting	Local via USB Flash drive. Remote via PC (with Ethernet and web browser capabilities)			
Audit log	21 CFR Part 11 and EU Annex 11 compliance enabled			
Integrated process monitoring				
RTD temperature sensor	Burns Engineering TE-01/A/B2			
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			
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	50 to 200 rpm			
Absolute min. volume	28 L	44 L	76 L	119 L
Absolute max. volume	110 L	220 L	550 L	1010 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 85%, noncondensing			
Cleaning agents	External surfaces of the system components are compatible with commonly used cleaning methods in GMP and lab environments			

[1] All specifications are subject to change without notice.

Table 4. Site preparation guide

		100 L	200 L	500 L	1000 L
1. Containers					
Minimal door aperture	XDUO Jacketed	840 mm (33.1 in)	980 mm (38.6 in)	1240 mm (48.8 in)	1400 mm (55.1 in)
	XDUO Non-jacketed	840 mm (33.1 in)	980 mm (38.6 in)	1240 mm (48.8 in)	1400 mm (55.1 in)
Total crate and unit weights	XDUO Jacketed	220 kg (485 lb)	280 kg (618 lb)	420 kg (926 lb)	570 kg (1257 lb)
	XDUO Non-jacketed	180 kg (397 lb)	220 kg (485 lb)	310 kg (684 lb)	440 kg (970 lb)
2. Uncrating the system					
Tools required		Forklift or pallet jack, screwdriver with #2 Phillips bit, small pry bar or large flat-head screwdriver			
3. Power requirements					
I/O cabinet supply voltage		100-120 VAC, 50 or 60 Hz, 1 phase, 4.5 A; 200-240 VAC, 50 or 60 Hz, 1 phase, 3.0 A			
Unit maximum power consumption		720 VA			
4. Transportation route					
Minimal door aperture	XDUO Jacketed	684 mm (26.9 in)	813 mm (32.0 in)	1016 mm (40.0 in)	1220 mm (48.0 in)
	XDUO Non-jacketed	574 mm (22.6 in)	700 mm (27.6 in)	903 mm (35.6 in)	1105 mm (43.5 in)

Single-use bags

Specifications of the single-use bags are listed in Table 5. Xcellerex Plus bag assembly connections are described in Table 6 below and in Figure 7.

Table 5. Specifications[1]

	100 L	200 L	500 L	1000 L
Single-use bags				
Dimensions (W × H × D)	508 × 483 × 508 mm (20 × 19 × 20 in)	635 × 610 × 635 mm (25 × 24 × 25 in)	838 × 813 × 838 mm (33 × 32 × 33 in)	1041 × 940 × 1041 mm (41 × 37 × 41 in)
Hold-up volume	< 20 mL			
Fluid contact layer (film material)	ULDPE (USP Class VI) for bags with PL-1026/PL-1077 film, LDPE (USP Class VI) for Fortem™ film bags			
Tubing material	C-Flex® 374 for bags with PL-1026/PL-1077 film, AdvantaFlex™ for Fortem film bags			
Sterilization	Dosed at 27.5 to 45 kGy for bags with PL-1026/PL-1077 film, 27.5 to 44 kGy for Fortem film bags			
Product recovery	> 99.9%			
Bag set-up time	< 5 min for one person			
Impeller				
Material	Marlex™ 0918 HDPE			
Number of blades	3			
Diameter	191 mm (7.5 in)			
Blade (W × H)	64 × 107 mm (2.5 × 4.2 in)			
Blade pitch	57°			

[1] All specifications are subject to change without notice.

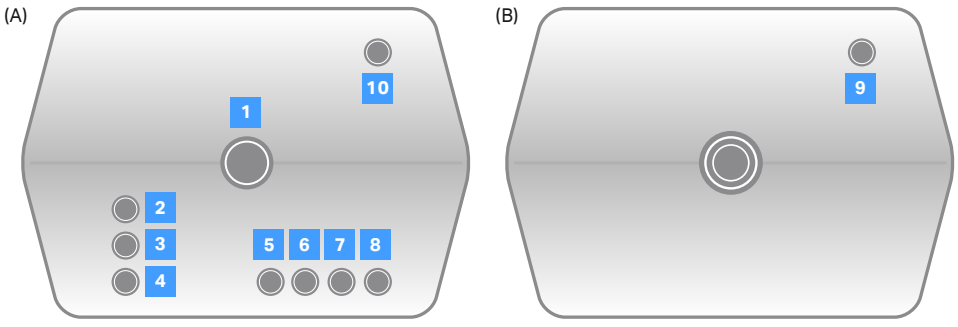


Fig 7. The (A) top and (B) bottom of Xcellerex XDM-500L Plus bags. Port positions 1 to 10 are described in Table 6.

Table 6. Xcellerex single-use bag assembly connections[1]

Port	Description	50 L	100 L	200 L	500 L	1000 L
Fortem bag assembly						
1	Fill port: 3" Tri-Clamp™ powder addition port, capped	×	×	×	×	×
2	Advantaflex tubing, 5' with clamp, plugged, ReadyMate™, or Aseptiquik G (ID indicated)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	19.1 mm (3/4 in)	19.1 mm (3/4 in)
3	1/8" i.d. Advantaflex tubing, 3' with clamp, plugged	NA	NA	NA	NA	NA
4	1/8" i.d. Advantaflex tubing, 3' with clamp, plugged	NA	NA	NA	NA	NA
5, 6	Probe port: Aseptiquik G connector port for probe connection	NA	NA	NA	NA	NA
7	Thermowell: for noninvasive temperature sensing	NA	NA	NA	NA	NA
8	Sample line: 1/8" i.d. sample line with clamp, and swabbable valve connection	×	×	×	×	×
9	Harvest/drain: Advantaflex tubing, 6' with clamp and plugged, ReadyMate, or Aseptiquik G (i.d. indicated)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	19.1 mm (3/4 in)	19.1 mm (3/4 in)
10	Advantaflex tubing, 5' with clamp, plugged, ReadyMate, or Aseptiquik G (ID indicated)	NA	NA	NA	NA	NA
Fortem plus bag assembly						
1	Fill port: 3" Tri-Clamp powder addition port, capped	×	×	×	×	×
2	Advantaflex tubing, 5' with clamp, plugged, ReadyMate, or Aseptiquik G (ID indicated)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	19.1 mm (3/4 in)	19.1 mm (3/4 in)
3	1/8" i.d. Advantaflex tubing, 3' with clamp, plugged	×	×	×	×	×
4	1/8" i.d. Advantaflex tubing, 3' with clamp, plugged	×	×	×	×	×
5, 6	Probe port: Aseptiquik G connector port for probe connection	×	×	×	×	×
7	Thermowell: for noninvasive temperature sensing	×	×	×	×	×
8	Sample line: 1/8" i.d. sample line with clamp, and swabbable valve connection	×	×	×	×	×
9	Harvest/drain: Advantaflex tubing, 6' with clamp and plugged, ReadyMate, or Aseptiquik G (i.d. indicated)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	19.1 mm (3/4 in)	19.1 mm (3/4 in)
10	Advantaflex tubing, 5' with clamp, plugged, ReadyMate, or Aseptiquik G (ID indicated)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	19.1 mm (3/4 in)	19.1 mm (3/4 in)
Standard bag assembly (PL-1026/PL-1077 film)						
1	Fill port: 3" Tri-Clamp powder addition port, capped	×	×	×	×	×
2	C-Flex 374 tubing, 4' with clamp, plugged or ReadyMate (ID indicated)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	19.1 mm (3/4 in)
3	1/2" i.d. C-Flex 374 tubing, 4' with clamp, female MPX connector, plugged	NA	NA	NA	NA	NA
4	1/8" i.d. C-Flex 374 tubing (36") with Luer lock connection	NA	NA	NA	NA	NA
5, 6	Probe port: female Kleenpak™ connector port for probe connection	NA	NA	NA	NA	NA
7	Thermowell: for noninvasive temperature sensing	NA	NA	NA	NA	NA
8	Sample line: 1/8" i.d. sample line with clamp, and Luer lock connection	×	×	×	×	×
9	Harvest/drain: C-Flex 374 tubing, 6' with clamp, plugged or ReadyMate (i.d. indicated)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	19.1 mm (3/4 in)
10	C-Flex 374 tubing, 4' with clamp, plugged or ReadyMate (i.d. indicated)	NA	NA	NA	NA	NA
Plus bag assembly (PL-1026/PL-1077 film)						
1	Fill port: 3" Tri-Clamp powder addition port, capped	×	×	×	×	×
2	C-Flex 374 tubing, 4' with clamp, plugged or ReadyMate (i.d. indicated)	19.1 mm (3/4 in)	19.1 mm (3/4 in)	19.1 mm (3/4 in)	19.1 mm (3/4 in)	19.1 mm (3/4 in)
3	1/2" i.d. C-Flex 374 tubing, 4' with clamp, female MPX connector, plugged	×	×	×	×	×
4	1/8" i.d. C-Flex 374 tubing (36") with Luer lock connection	×	×	×	×	×
5, 6	Probe port: female Kleenpak connector port for probe connection	×	×	×	×	×
7	Thermowell: for noninvasive temperature sensing	×	×	×	×	×
8	Sample line: 1/8" i.d. sample line with clamp, and Luer lock connection	×	×	×	×	×
9	Harvest/drain: C-Flex 374 tubing, 6' with clamp, plugged or ReadyMate (i.d. indicated)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	19.1 mm (3/4 in)
10	C-Flex 374 tubing, 4' with clamp, plugged or ReadyMate (i.d. indicated)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)	12.7 mm (1/2 in)

[1] All specifications are subject to change without notice. Table refers to all bags.

Ordering information

	Product codes			
Bags	**100 L**	**200 L**	**500 L**	**1000 L**
Fortem	29301275	29299915	29304524	29297664
Fortem Plus	29280674	29282860	29305463	29296403
Fortem with ReadyMate	29395000	29395002	29395004	29395006
Fortem Plus with ReadyMate	29395001	29395003	29395005	29395007
Fortem with Aseptiquik	29395107	29395109	29395111	29395113
Fortem Plus with Aseptiquik	29395108	29395110	29395112	29395114
Standard	888-0164-C	888-0165-C	888-0166-C	888-0167-C
Standard with ReadyMate	888-0164-F	888-0165-F	888-0166-F	888-0167-F
Plus	888-0154-C	888-0155-C	888-0156-C	888-0157-C
Plus with ReadyMate	888-0154-F	888-0155-F	888-0156-F	888-0157-F

Xcellerex XDUO Mixers	
Jacketed	29054862
Non-jacketed	29054861

Accessories	
Assure probe sheath (4)	29207815
Probe sheath (4)	29041158
XDM 50 basic tote	29041160
Sample manifold (2)	29041165
Sample manifold (4)	29041166
Sample manifold (10)	29041167
5 kg Fortem film powder bag	29399774
10 kg Fortem film powder bag	29399775
5 kg powder bag	29041168
10 kg powder bag	29041169
Probe clamp pliers	29041784
XDM hopper	29056423
Insert pH, 12 × 225 mm, Hamilton, VP	817-00144
Insert conductivity, 12 × 225 mm	817-80003
Reusable probe stand autoclave	826-00304

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