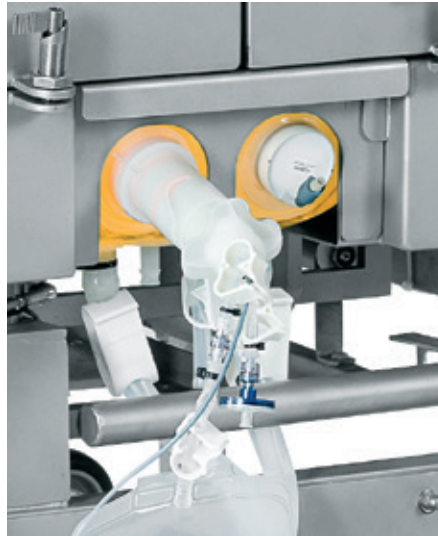




Standard Flexel[®] for LevMixer[®]

with Single-use pH Sensor, Single-use Conductivity Sensor and Thermowell



Typical Applications

Flexel[®] for LevMixer[®] with pH sensor and thermowell:

- Dilution prior to chromatography,
- Low pH virus inactivation,
- pH adjustment of column eluate,
- Protein re-folding,
- Product formulation.

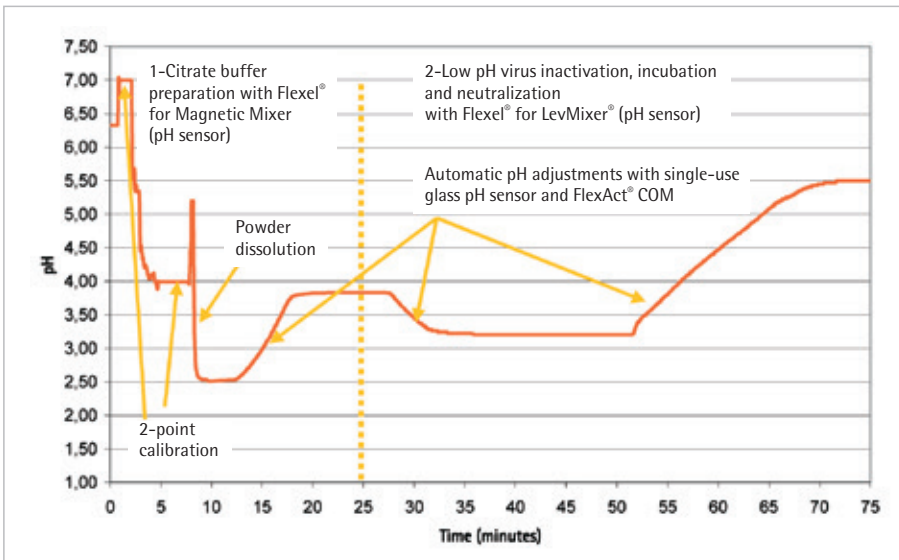
Flexel[®] for LevMixer[®] with pH sensor, conductivity sensor and thermowell:

- Ultrafiltration | Diafiltration
- Intermediate and Final product formulation

Description

pH, conductivity and temperature are key process parameters within many biopharmaceutical unit operations, for which sample withdrawal or external probe's insertion may result in possible cross contamination or biohazard exposure.

Flexel[®] for LevMixer[®] (1) with pre-assembled pH sensor, conductivity sensor and thermowell is an innovative single-use solution providing ultra-clean mixing, with in-line monitoring or control of the pH, the conductivity and the temperature from 50 L to 1,000 L.



Example of in-line pH monitoring and control with 200 L Flexel[®] for Magnetic Mixer⁽²⁾ (buffer preparation) and 200 L Flexel[®] for LevMixer[®] (virus inactivation)

Product Features & Benefits

Single-use pH sensor

Features	Benefits
Pre-installed and pre-sterilized single-use pH sensor	Eliminates contamination risk compared to re-usable sensor. Eliminates operator exposure to biohazardous substances. Reduces process cycle time (no autoclaving)
Wet storage of electrode in HDPE compartment	Robust electrode protection and long-term stability (1 year shelf-life)
Electrochemical pH sensor	Real-time pH reading for accurate dosing up to 1,000 L.
Single-use pH sensor connected to hand held pH-meter	In-line pH monitoring (no need for QC sampling)
Single-use pH sensor connected to FlexAct® COM	Automated pH adjustment with FlexAct® BP, MP or VI Reduces process cycle time and risk of pH overshoot
Large measurement range pH2 – pH11	Compatible with most biopharmaceutical applications
High accuracy after 2 points calibration pH2 – pH9; 10°C – 40°C: ±0.1 pH3 – pH7; 25°C: ±0.05	Compatible with most pH sensitive applications
Retractable Probe (3 activations authorized with maintained sterility)	Sterile in-process 2 nd calibration or post-use pH verification

Single-Use Conductivity sensor

Features	Benefits
Pre-installed and pre-sterilized single-use conductivity sensor	Avoids sample withdrawal or external probe's insertion Eliminates contamination risk compared to re-usable sensor.
Pre-calibrated single-use conductivity sensor	Ready to use
4 electrodes system with an integrated temperature sensor (Pt1000)	Real conductivity measurement
Single-use conductivity sensor connected to: – Hand held conductivity-meter – FlexAct® COM – 3rd party automation (direct connection via an open ends plug)	In-line conductivity measurement with large offering for conductivity reader
Large measurement range 100µS/cm up to 200 mS/cm	Compatible with most biopharmaceutical applications
Accuracy <100mS/cm: 2% 100mS/cm – 200mS/cm: 5%	Accurate conductivity measurement

Thermowell (thin silicone sleeve) for insertion of reusable temperature sensor

Features	Benefits
3.2 mm ID thermowell for re-usable temperature sensor's insertion	Non-invasive and accurate temperature measurement for pH compensation. Prevent from cross contamination risk or biohazard exposure.

Standard Flexel® Bag for LevMixer® with pH, conductivity and thermowell

Features	Benefits
Volumes from 50 L to 1,000 L	Covers most process development and GMP downstream unit operations. Custom from 1,500 L up to 3,000 L designs available with pH and or conductivity and or thermowell
Contact-free impeller rotation (levitated impeller)	Low-shear mixing for sensitive products as well as ultra-clean conditions up to 1,000 L
Full compliance with ISO 11137	Highest sterility assurance level
Full compliance with USP <788> after rotation in aqueous solution	Provides clean operations for mixing of aqueous agents
Standard bag designs	Improved delivery time compared to custom designs

Components

Flexel® for LevMixer® with pH, conductivity and thermowell sensors is an innovative single-use mixing solution using the ATMI patented Mixing Technology and Sartorius Stedim Biotech Flexel® Bag, transfer sets, Palletank® and sensor technologies.

1. Palletank® from 50 L to 1,000 L for impeller mixing:

Palletank® for LevMixer® is a stainless steel cubical container designed to perfectly fit with the Flexel® Bag for LevMixer® with its integrated impeller and single-use sensors. It includes a railed port for coupling a mobile LevMixer® Drive Unit with the Palletank®. The hinged door allows easy installation of the bag system whereas the front bottom gate facilitates tubing and sensor installation and calibration. Windows on lateral and rear sides enable the user to visually inspect the mixing process. The cubical shape facilitates the manipulation and improves the mixing efficiency to offer scalability from 50 L to 1,000 L. Load cells for accurate weight monitoring and double wall, insulated jacket for cooling and heating applications are available as standard options (please consult the corresponding datasheets).

2. LevMixer® Drive Units generates the levitation and rotation of the single-use impeller without surface contact. The drive units are mobile, cart-mounted and designed to interface with any standard Palletank® from 50 L to 1,000 L (please consult the corresponding datasheets).

3. Flexel® Bag for LevMixer® with conductivity sensor, pH sensor and thermowell:

From 50 L to 1,000 L: Flexel® Bag for LevMixer® contains an in center magnetic impeller assembly, a single-use conductivity sensor, single-use pH sensor and a thermowell for 3.2 mm OD temperature probe insertion. Its cubical design simplifies installation and facilitates the unfolding and folding of the bag during filling and draining operations. The patented protection cap provides robustness avoiding contact of the impeller with the film during transport. It also offers a large diameter port for powder transfer. Two new top lines have been designed for connection of standard transfer sets to perform contained acid | base addition.

4. Single-use pH sensor is provided pre-installed and pre-sterilized with the Flexel® Bag for LevMixer®. The single-use pH sensor comprises a pH glass electrode stored in an HDPE compartment and equipped with a flow cell for 2-point calibration at the point of use. This device is designed to isolate the electrode from the bag interior during storage and calibration and to insure sterile insertion of the electrode inside the bag following calibration. 3 activations (2 insertions, 1 withdrawal) are authorized to maintain sterility into the bag. The glass pH electrode is supplied in pH 6.5 sterile, gamma-stable, buffered conservation solution. Sterility is maintained with a 0.2 µm syringe filter at the inlet and a pre-connected waste bag at the outlet of the flow cell.



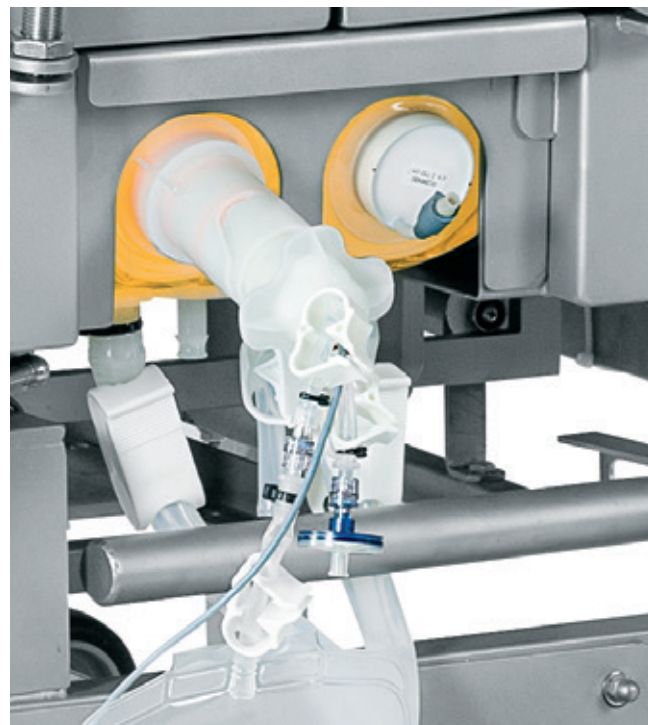
Single-use pH sensor with thermowell on Flexel® Bag for LevMixer®

5. Two transfer sets are specifically designed for contained acid or base addition after connection to the top of the Flexel® Bag for LevMixer® with single-use pH sensor.

Two lengths (4 or 5 meters) are qualified to allow mixing bag emptying without lines disconnection (no operator's exposure to chemicals).

Diameters are chosen for pumping with Watson Marlow dosing pump WM 520U/R2 on either a 1/4" ID silicone tubing or 1/8" ID silicone tubing depending on accuracy required by the process.

6. Single-use conductivity sensor is provided pre-calibrated, pre-installed and pre-sterilized with Flexel® Bag for LevMixer®. The Single use conductivity sensor is composed by a HDPE housing where inside a thick film system is sealed into a ceramic module. The device is based on a 4 electrodes system with an integrated temperature sensor (Pt1000). The sensor is precalibrated and each sensor has its individual cell constant (calibration factor) on the back side.



Single-use pH sensor and single-use conductivity sensor on Flexel® Bag for LevMixer®

Validation

Flexel® Bags for LevMixer® with sensors have been qualified applying the most stringent and innovative test regimes. Biological, chemical and physical tests combined with extensive extractable testing provide users of Flexel® Bags for LevMixer® with data representing the widest range of process fluids in a variety of processing conditions.

Full compliance with ISO11137 allows for a validated claim of sterility on all Sartorius Stedim Biotech Single-Use Products with a sterility assurance level of 10^{-6} over the shelf life.

Flexel® Bags for LevMixer® and their components are tested for compliance to:

- USP <87>: Biological reactivity tests, in Vitro
- USP <88>: Biological reactivity tests, in Vivo
- USP <661>: Containers-Physicochemical tests – Plastics
- USP <788> Particulate matter in injections – Large-volume injections and E.P. 2.9.19: Particulate contamination-sub-visible particles
- USP<85> and EP 2.1.14: Bacterial endotoxins test
- ISO 11737: Microbiological methods-Determination of a population of microorganisms on products
- ISO 11137: Sterilization of Health care products-Radiation

Specifically, single-use pH and conductivity sensors are qualified after Gamma irradiation for:

- Resistance to pressure (leak tests)
- Mechanical resistance
- Application tests for pH sensor, including technical notes as follows:
 - Volumes of standard buffer solution for two-point calibration with Flexel® for LevMixer® | Magnetic Mixer
 - Real time pH adjustments with FlexAct® Central Operating Module
 - Exposure to buffer solution over time.
- Application tests for conductivity sensor, including technical and application notes as follows:
 - Temperature Effects on SU conductivity sensor used with Flexel® for LevMixer® | Magnetic Mixer
 - Conductivity measurement in Single-Use mixing applications

Quality Assurance

Sartorius Stedim Biotech Quality Systems for Single-Use Products follow applicable ISO and FDA regulations. Design, manufacture and sterilization processes are conducted under conditions that mirror biopharmaceutical operations and meet cGMP requirements.

Security of Supply

Sartorius Stedim Biotech has established multiple manufacturing sites with consistent industrial processes. The expertise of designing single-use solutions with a collaborative supplier management and customer demand planning assures a state-of-the-art and robust supply chain that can cope with strong market growth.

Specifications

1. pH glass electrode

Sensor	Electrochemical pH glass electrode
Measurement range	pH 2 to 11
Accuracy	pH2 – pH9; 10°C – 40°C: ±0.1 pH3 – pH7; 25°C: ±0.05
Probe Holder	Inlet: 0.2 µm Minisart® Syringe Filter Outlet: 1 L waste bag Main body and sensor holder: HDPE O-ring gaskets: Silicone
Cable & Connector	2 m cable with DIN connector (DIN/BNC adapter FMA114320 available on demand)
Storage Solution	pH = 6.5 ± 0.3, sterile buffered conservation solution
Sterilization	by Gamma irradiation (pre-assembled to bag assembly)

2. Single-Use Conductivity sensor

Sensor	4 electrodes system with an integrated temperature sensor (Pt 1000)
Measurement range	100 µS/cm to 200 mS/cm
Accuracy	2% <100 mS/cm 5% 100 mS/cm – 200 mS/cm
Probe Holder	HDPE Housing Thick film sealed into a ceramic module
Cable & Connector	– BPT0031: cable Conductivity DCU – BPT0032: cable Conductivity open ends (direct connection to 3rd party automation) – BPT0033: cable Conductivity Knick handheld
Sterilization	by Gamma irradiation (pre-assembled to bag assembly)

3. Flexel® Bag for LevMixer® – 50 L to 1,000 L

Bag Chamber	Flexel® Bag with multi-layer film, including EVOH gas barrier layer and PE contact layer
Impeller Position	Bottom centered
Impeller Size	126 mm (4.95") for 50 L and 100 L (HDPE) 161 mm (6.35") from 200 L to 1,000 L (HDPE)
Tubing Material	TUflux® SIL, Silicone, TPE
Number of Ports	2 top ports for acid/base addition, 1 large top port for powder addition, 4 front bottom ports.

Fittings	MPC MPX Quick Connect Coupling with plug, Tri-clamp with plug, Needless sampling port
Thermowell	3 mm ID – 135 mm length silicone sleeve with High Density Polyethylene (HDPE) port
Single-use pH sensor assembly	Electrochemical pH glass electrode Insertion device composed of high density Polyethylene (HDPE) and silicone components
Single-use conductivity sensor	4 electrode system with an integrated temperature sensor HDPE housing and film sealed into a ceramic module
Volumes	50 L, 100 L, 200 L, 400 L, 650 L and 1,000 L
Nominal Filling Volume	Minimum(*) – Maximum Volume
50 L	30 L – 60 L
100 L	40 L – 110 L
200 L	60 L – 230 L
400 L	120 L – 420 L
650 L	160 L – 720 L
1,000 L	250 L – 1050 L
	(* under aseptic conditions = worst case scenario) For optimization of the minimum volume for mixing: contact your local application specialist.
Sterilization	by Gamma irradiation

4. Palletank® for LevMixer®

Please consult the datasheet "Standard Flexel® for LevMixer®
50 L to 1,000 L"

5. LevMixer® Drive Unit

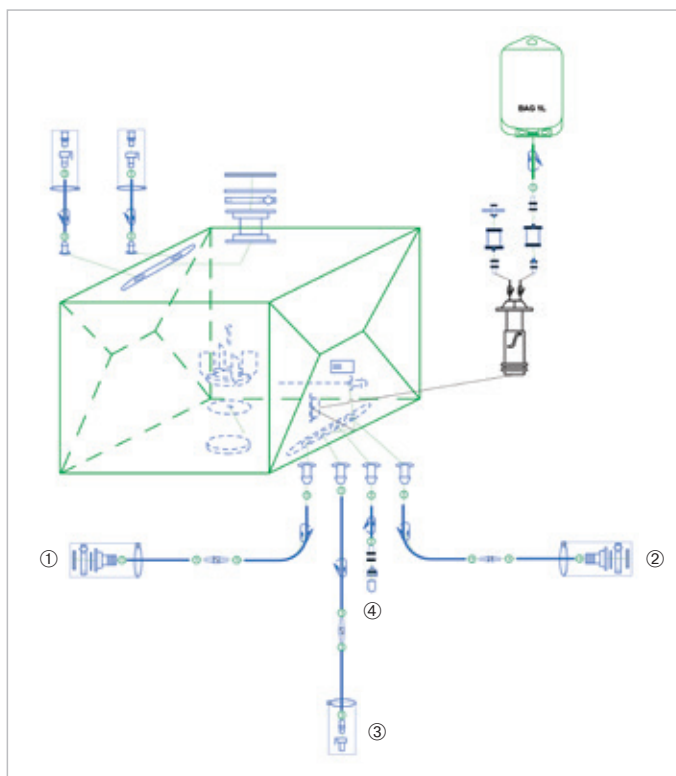
Please consult the datasheet "Standard Flexel® for LevMixer®
50 L to 1,000 L"

6. Transfer sets for pH adjustments

Length	– 4 meters: connection to 50 L, 100 L, 200 L Flexel® Bag for LevMixer® – 5 meters: connection to 400 L, 650 L, 1,000 L Flexel® Bag for LevMixer®
Tubing Material	Silicone
Tubing Diameter	1/4" × 7/16" 1/8" × 5/16"
Fittings	Inlet: Female MPC Quick Couplers with plug (possible connection to Flexboy®) Outlet: Male MPC Quick Couplers with plug (connection to top of Flexel® Bag for LevMixer® with single-use pH sensor)

Ordering Information

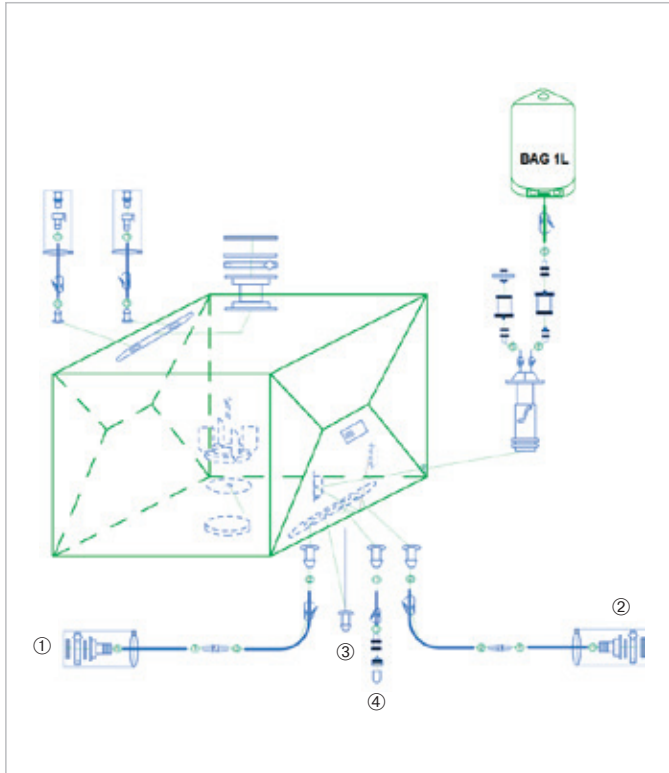
1. Flexel® Bag for LevMixer® with pH sensor and thermowell (50 L to 1,000 L)



Line	Function	Tubing material	Tubing diameters and length	End Connector
Line 1	Fill	Silicone + TPE	1/2" x 3/4" x 1.5 m (60")	1-1/2" Tri-Clamp with cap
Line 2	Drain	Silicone + TPE	1/2" x 3/4" x 1.5 m (60")	1-1/2" Tri-Clamp with cap
Line 3	Addition	Silicone + TPE	1/2" x 3/4" x 1.5 m (60")	1/2" MPX male + sealing cap
Line 4	Addition Sampling	Silicone	1/4" x 7/16" x 0.1 m (4")	LL female + needle free sampling port
Top lines	Addition (Titration)	Silicone	1/4" x 7/16" x 0.1 m (4")	1/2" MPC female + sealing cap

Part Number	Description	Qty/Box
FMB113993	STD Flexel® Cubical for LevMixer® 50 L Probe pH, TPE	2
FMB113994	STD Flexel® Cubical for LevMixer® 100 L Probe pH, TPE	2
FMB113995	STD Flexel® Cubical for LevMixer® 200 L Probe pH, TPE	2
FMB113996	STD Flexel® Cubical for LevMixer® 400 L Probe pH, TPE	2
FMB113997	STD Flexel® Cubical for LevMixer® 650 L Probe pH, TPE	1
FMB113998	STD Flexel® Cubical for LevMixer® 1,000 L Probe pH, TPE	1

2. Flexel® Bag for LevMixer® with pH sensor, conductivity sensor and thermowell (50 L to 1,000 L)



Line	Function	Tubing material	Tubing diameters and length	End Connector
Line 1	Fill	Tuflux® SIL + TPE	1/2" x 3/4" x 1.5 m (60")	1-1/2" Tri-Clamp with cap
Line 2	Drain	Tuflux® SIL + TPE	1/2" x 3/4" x 1.5 m (60")	1-1/2" Tri-Clamp with cap
Line 3	Thermowell	-	-	-
Line 4	Addition Sampling	Tuflux® SIL	1/4" x 7/16" x 0.1 m (4")	LL female + needle free sampling port
Top lines	Addition (Titration)	Tuflux® SIL	1/4" x 7/16" x 0.1 m (4")	1/2" MPC female + sealing cap

Part Number	Description	Qty/Box
FMB122496	STD Flexel® Cubical for LevMixer® 50 L (TPE/Probe pH/Cond)	2
FMB122497	STD Flexel® Cubical for LevMixer® 100 L (TPE/Probe pH/Cond)	2
FMB122498	STD Flexel® Cubical for LevMixer® 200 L (TPE/Probe pH/Cond)	2
FMB122499	STD Flexel® Cubical for LevMixer® 400 L (TPE/Probe pH/Cond)	2
FMB122500	STD Flexel® Cubical for LevMixer® 650 L (TPE/Probe pH/Cond)	1
FMB122501	STD Flexel® Cubical for LevMixer® 1,000 L (TPE/Probe pH/Cond)	1

3. Single-use pH sensor accessories

Part Number	Description	Qty/box
FMA114320	Component DIN BNC Adapter pH Probe	1
BB-8840050	3.2 mm OD temperature probe for thermowell (2.5 mm phone plug)	1
FBT116668	STD Transfer set MPC MPC – length 4 meters	5
FBT116669	STD Transfer set MPC MPC – length 5 meters	5

4. Single-use conductivity sensor accessories

Part Number	Description	Qty/box
BB 8800005	Knick handheld portamess 913	1
BPT0031	Cable Conductivity DCU	1
BPT0032	Cable Conductivity open ends (direct connection to 3rd party automation)	1
BPT0033	Cable Conductivity Knick handheld	1

5. Palletank® for LevMixer®

Please consult the datasheet "Standard Flexel® for LevMixer® 50 L to 1,000 L"

6. LevMixer® Drive Unit

Please consult the datasheet "Standard Flexel® for LevMixer® 50 L to 1,000 L"

⁽¹⁾ LevMixer® is a trademark or registered trademark of ATMI, inc in the United States, other countries or both and this product uses ATMI patented LevMixer® technology.

⁽²⁾ This product uses ATMI patented Magnetic Mixer technology.

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