

# M series

## SIP&CIP Standard Pilot Scale Fermenters/Bioreactors

### Scope of Supply

This technical proposal describes a Solaris M-Series M-30.

The system consists of the pre-assembled 30 L fermenter/bioreactor (total volume) and control cabinet mounted on a stainless-steel frame & is supplied with all necessary piping, valves, instrumentation, automation controls and HMI. The system is designed for closed aseptic aerobic or anaerobic cultivations/fermentations. The system is fully suitable for inline CIP and SIP. Control is based on PLC & SCADA system.

### Example of M series



## Vessel

Vessels/heat exchangers are designed, fabricated, inspected, documented, and tested in accordance with European PED.\*

\*further certifications available upon request

### Volume

- Total Volume: 30 l
- Maximum Working volume: 22.5 l

### Ratio H:D

- 3 : 1

### Design

- Cylindrical vertical vessel supported on 3 tubular short legs flanged on a movable skid on wheels.
- Flat lid and totally drainable dished bottom.
- Jacket on vessel body and bottom.

### Materials

- All parts in contact with the culture are in AISI 316 L
- Vessel: AISI 316 L
- Other parts in AISI 304
- Sight glass: Borosilicate
- Materials are guaranteed by origin certificates, chemical analysis and mechanical characteristics.
- Gaskets are FDA approved materials: EPDM and silicone

### Finishing

- All parts in contact with the culture:  $Ra < 0,4 \mu m$
- External: mirror polished

### Operating conditions

- Vessel project pressure: -1/+4.0 bar
- Jacket project pressure: -1/+5.5 bar
- Vessel project temperature: 0-152 °C
- Jacket project temperature: 0-162 °C

M30 connections		
Position	Qty	Description
Vessel lid	n.2	Lifting hoops
	n.3 DN12 PG13.5	Spare (Level, A.F., etc.)
	n.7 TK ¾"	Safety Valve, Gas-out, Pressure probe
		SALAS - Solaris Sterile Liquid Addition System Steam-bridge (n.2)
		Sight Glass with lamp
		n.4 spare (steam bridge)
	n.1	Stirring group
Upper side wall	n. 1 TK ¾"	Overlay gas inlet
	n.1	Sparger
	n.2 TK 1"	Spare (spray ball)
	n.1	Elliptical sight glass
Lower side Wall	n.5 Hygienic Socket Solaris	Temperature + n.4 spare (for pH, dO2. etc.)
	n. 1 TK ¾"	Sampling
	n.1 TK 1"	Spare (spray ball)
Vessel Bottom	n. 1 TK ¾"	Harvest valve
Jacket in-out	n. 1 TK ¾"	Jacket in
	n. 1 TK ¾"	Jacket out

## Utilities and characteristics

Utilities	Requirement	Connections
Electrical	Power supply 380-400 Vac, 50/60 Hz	Standard industrial connector UEC 16A 5 poles (3P+N+GND)
Gas: Air (or other gases) for mass flow meter	2,5 bar(g), oil free compressed	½" Gas male
Instrument air	6,0-6,5 bar (g)	Quick connection For tube 4 x 6 mm
Jacket Empty Air	1,0 bar(g), oil free compressed	Quick connection For tube 4 x 6 mm
Cooling Water (Inlet)	1,0-1,5 bar(g)	½" Gas male
HP Steam	2,5-3,0 bar (g)	½" Gas male
LP Steam	1,5-2,0 bar (g)	½" Gas male
Exhaust	Open	
Water Out (Drain)	Open Drain	½" Gas male
Condensate drain	Open drain	½" Gas male

## Agitation System

Position:	Top flanged
Type:	Mechanical coupling
Impellers:	n.3, 6 blades disc Rushton type impellers or n.2 Marine Impellers (adjustable in height and removable)
Project Press:	-1/+3.0 bar
Project Temp:	-10 / 150 °C
Viscosity:	100 mPas
Density:	1100 kg/m <sup>3</sup>
Material (product contacted):	AISI 316

### Mechanical seal

The standard M-Series mechanical seal is a single type, consisting of a rotating ring and stationary ring. The second ring rotates on the first ring under spring load. This type of mechanical seal, taking consideration of the materials of construction, requires lubrication

that reduces the friction between the dragging surfaces also preventing excessive heat buildup.

#### Double mechanical seal (Option)

Double mechanical seal lubricated with sterile steam condensate, generated by the heat exchanger and automatically circulated.

Materials: FDA approved tungsten/silicon carbide

#### Baffles

The fermenter/bioreactor is fitted with 4 welded baffles (90°) on the vessel's internal wall.

### Gas in

Gas in entering through overlay and sparger.

#### Sparger

n.1 removable toro type (ring) or removable sintered type(micro bubbling) included

#### Gas in filters

- The fermenter/bioreactor is fitted with sterilizing filters for the process incoming gas (sparger and overlay).
- The filter cartridge consists of a PTFE membrane with 0.2 microns porosity, contained within a pressure casted polypropylene armature that can be repeatedly sterilized at 121°C.
- The cartridge is inserted into a stainless-steel container through a Tri-Clamp connection.
- The container has connections for air inlet/outlet, automatic condensation discharge and manometer (optional) installation.

#### Temperature measurement on Gas In filter sterilization (option)

Temperature probe could be fitted on the drain condensate line under gas in filter. The probe records the temperature (trend available on HMI), and validates the sterilization process.

### Gas out

#### Gas out filters (option)

- The fermenter/bioreactor is fitted with sterilizing filters for outlet gas (option) with

temperature measurement (option).

- The filter cartridge consists of a PTFE membrane with 0.2 microns porosity, contained within a pressure casted polypropylene armature that can be repeatedly sterilized at 121°C.
- The cartridge is inserted into a stainless-steel container through a Tri-Clamp connection.
- The container has connections for air inlet/outlet, automatic condensation discharge and manometer (optional) installation.

#### Temperature measurement on gas out filter sterilization (option)

Temperature probe could be fitted on the drain condensate line under gas in filter. The probe records the temperature (trend available on HMI), and validates the sterilization process.

#### Reflux Cooler (option)

Before the outlet filter a Reflux Cooler (condenser) could be included to prevent media loss.

### Inoculums/Feedings/pH corrective solutions/A.F solution

#### SALAS - Solaris Sterile Liquid Addition System

The fermenter/bioreactor is supplied with a 4 channels **SALAS** valve for needle free additions.

#### Resterilizable addition (Steam Bridge) system (option) – up to 2

The inoculum, feeding and pH control inlets are connected through a group of 4 sanitary manual or automatic diaphragm valves, with an in-line reference temperature sensor (only on automatic), that can be sterilized (steam bridge) independently from the vessel.

A steam bridge line consists of:

- 4 group steam bridge diaphragm valves systems, manual or automatic
- Steam trap
- T °C sensor (only on automatic)
- Sterilization sequence through software (only on automatic)

### Sampling and Harvest valves

The fermenter/bioreactor is fitted with a sampling valve located on lower side wall for process sampling, and a harvest valve located on the vessel bottom for full harvesting.

### Manual or automatic re-sterilizable Sampling and Harvest valves (option)

The fermenter/bioreactor could be fitted with a manual or automatic sterilization system for sampling and harvest valves, that can be sterilized independently from the vessel (*in the standard configuration, sampling and harvest valves are not re-sterilizable with clean steam*).

Sterilization sequence occurs through manual or pneumatic diaphragm valves with temperature measurement (only for automatic). The probe records the temperature (trend available on HMI), and validates the sterilization process.

### Peristaltic Pumps (option)

Each system could be supplied with different type and number of peristaltic pumps, application configurable from software:

- Pump can be activated manually or automatically
- Pumps can be utilized on duty cycle (timer), PID control or at a set rate

Pumps Model (fixed speed):

- Watson Marlow 114FD/DV; 60 rpm; up to 50 ml/min
- Watson Marlow 313 FDM 12/24VDC; 175 rpm; up to 1750 ml/min
- Watson Marlow 520FDM/R; 230 rpm 24V DC up to 3450 ml/min

### Gravimetric Flow Control

The system could be fitted with a Gravimetric Flow Control, which consists of:

- load cell for bottle of feeding
- bottle of feeding (various sizes: 3/5/10 l)
- Measuring & Control resident in Leonardo software

(at least n.1 peristaltic pump is required)

The feed rate is controlled through weight measurement. The bottle of feed, placed on a balance/load scale, is linked to a peristaltic pump. The user can enter a feed set point on the software.

## Sterilization

The fermenter/bioreactor can be sterilized with media, or empty (option). Sterilization is performed by automatically controlled SIP sequences. Filters are sterilized simultaneously with the fermenter/bioreactor.

Sterilization can be performed with steam or electrical heating(option).\*

\*In the configuration with electrical heating, clean steam is required for all peripheral devices sterilization (ex. Steam bridge, sampling/harvest valves, mechanical seal) and for empty vessel sterilization.

### Vessel Empty Sterilization (Option)

Empty sterilization sequence could be integrated into the software. Clean steam is injected directly into the vessel through a pneumatic diaphragm valve.

## Measurement and control equipment included

### Agitation RPM control - 0.5 rpm accuracy

The system for the measure and control of agitation speed is composed by:

- Brushless DC Motor
- Measuring and Control resident in the Leonardo software
- Driver located inside the control module

### Gas flow – Gas mixing (TMFC from Bronkhorst accuracy 1% FS)

Gasses can be introduced through sparger and overlay inlet.

The automated system for measuring and controlling the gas flow is composed of:

- n.1 Thermal Massflow Controller (2 VVM - air)
- Measuring & Control resident in the Leonardo software

### Pressure (accuracy 0.05 bar(g))

The system is fitted with an automatic pressure control consisting of:

- Sterilizable pressure probe.
- Pressure control valve on vent line.
- Measuring & Control resident in Leonardo software



### Temperature control

Temperature control is accomplished via a PID controller, which uses input from the Pt100

The system is fitted with an automatic temperature control consisting of:

- Pt100 temperature probe
- Thermoregulation loop: n.2 heat exchangers, recirculating pump, valves.
- Measuring & Control resident in Leonardo software

Thermoregulation can be performed with steam or electrical heating (option) for heating, and chilled water for cooling.

### Available Measurement and Control options

#### pH Control (accuracy 0.03-0.05)

pH Measurement and Control consists of the following items:

- Sensor: combined type pre-pressurized glass-gel electrode
- Measuring & Control resident in Leonardo software (PID)
- pH adjustment: peristaltic pumps for addition of acid/basic, or via gas sparger\*

\*at least n.1 peristaltic pump is required

#### Dissolved Oxygen control

The automatic measurement and control system for dissolved oxygen consists of the following components:

- Sensor: n.1 optical electrode
- Automatic Cascade Control (resident in Leonardo software system) on RPM, Gas Control, feedings, etc.

#### Foam Control (Solaris)

The system for detection and control of the foam level consists of the following components:

- n.1 sensor: conductive probe
- Amplifier
- Detection & Control resident in Leonardo software

Anti-foam addition by peristaltic pumps (at least n.1 peristaltic pump is required).

#### Level control (Solaris)

The system for detection and automatic control of the level consists of the following

components:

- n.1 sensor: conductive probe (adjustable length)
- Amplifier
- Detection & Control Leonardo software

#### Gas mixing (option1)

The system can be configured for automatic rationing of gases (2/3/4) utilizing a thermal mass flow controller (included) and n.4 solenoid valves for a sequential introduction of gasses.

The system can work as O<sub>2</sub> enrichment or as a gas mixing system allowing the precise dosing of each individual gas. The air inlet can also be used for nitrogen (anaerobic processes).

#### Gas mixing (option2)

- Gas mixing with 2, 3, 4 Mass flow Controllers (one for each gas)
- Measurement and Control resident in Leonardo software system

#### Redox measurement

Redox Measurement consists of the following components:

- Sensor: combined type pre-pressurized glass-gel electrode
- Measurement resident Leonardo software system

#### Conductivity measurement

Conductivity Measurement consists of the following components:

- Sensor: Contained in stainless steel housing
- Measurement resident in the Leonardo software

#### Weight measurement

Weight measurement system consists of the following components:

- Measurement resident in the Leonardo software
- Sensor: n.3 load cells
- Signal converter

#### CO<sub>2</sub> measurement

CO<sub>2</sub> Measurement consists of the following components:

- Sensor: analog sensor
- Amplifier: Electrode connected to a signal amplifier situated in the control and power module.
- Measurement resident in Leonardo software

### Cell Density Measurement

#### Option 1 (total cell density)

Measurement parameter via Dencytee OD sensor:

The total cell density measurement is based on optical density utilizing NIR wavelength light. All suspended particles within the optical path absorb the generated light and can be correlated to total cell density. The Dencytee sensor maintains a constant light intensity at the detector, by varying the source intensity, which measurement is based from. This improves the linear range of measurement.

Light Source	LED
Measurement Principle	NIR
Measuring Range 1	$10^5$ to $7 \times 10^8$ mammalian cells/ml
Measuring Range 2	0.5 to 300 g/l dry weight (fermentation)

#### Option 2 (viable cell density)

Measurement parameter via Incyte capacitance/permittivity sensor:

The viable cell density measurement is based on capacitance/permittivity – dielectric spectroscopy theory of measurement. Viable cells, subject to an alternating electric field within a particular range of frequencies, can behave like capacitors via alternating polarization. The permittivity signal produced can be correlated to the viable bio-volume. Only viable cells are polarized in the alternating electrical field, allowing this method to be insensitive to dead cells, debris, etc.

Accuracy:	$\pm 5 \times 10^4$ cells/ml
Accuracy:	$\pm 0.05$ g/l dry weight (fermentation)
Conductivity Range	2 - 50 mS/cm (medium)
Measuring Range 1:	$5 \times 10^5$ to $8 \times 10^9$ mammalian cells cells/ml
Measuring Range 2:	5 to 200 g/l dry weight (fermentation)

- Mammalian cells including CHO, HEK-293, HeLa, SF-9
- Stem cells
- Yeast including *Pichia pastoris* and *stipitis*, *Saccharomyces cerevisiae*
- Fungi both filamentous and as pellets, like *Aspergillus niger*
- Bacteria like *Lactococcus lactis*, *E. coli*

## Chiller (Option)

Chiller data sheet	
Working temperature range	-5 – 25 °C
Ambient temperature range	-15 – 50 °C
Temperature stability	± 2 K
Volume water reservoir	19 L
Cooling output at 25 °C water outlet temperature	6.90 kW
Cooling output at 20 °C water outlet temperature	6.90 kW
Cooling output at 15 °C water outlet temperature	5.90 kW
Cooling output at 10 °C water outlet temperature	4.90 kW
Cooling output at 5 °C water outlet temperature	4.10 kW
Cooling output at 0 °C water outlet temperature	3.40 kW
Cooling output at -5 °C water outlet temperature	2.80 kW
Application	External
Noise level	50.40 dB(A)
Power consumption	1.80 kW
Pump pressure max.	3.40 bar
Pump flow max. (pressure)	42 L/min
Pump connection thread	Rp 1/2"

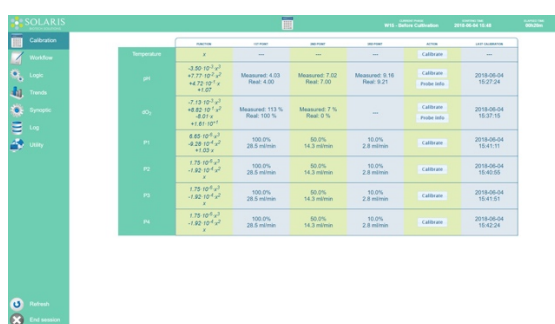
## Measurement and control system

The M-series system is fitted with a measurement and control system based on an SCADA supervisory platform connected through Ethernet and a Siemens PLC.


The HMI is an industrial touch screen PC. The monitor is used for monitoring and managing the M-Series system (touch screen or via mouse/keypad).

The system is provided with an open interface for the customer's DCS.

## LEONARDO 3.0: user friendly software

Parameter	Measured	Real	Calibrated	Calibration Date
Temperature	23.00 °C	23.00 °C	23.00 °C	2018-08-04 15:27:24
pH	7.77	7.77	7.77	2018-08-04 15:27:24
DO2	100.00 %	100.00 %	100.00 %	2018-08-04 15:27:24
Stirring Speed	100.00 %	100.00 %	100.00 %	2018-08-04 15:27:24
Air Flow	1.00 l/min	1.00 l/min	1.00 l/min	2018-08-04 15:27:24



Parameter	Measured	Real	Calibrated	Calibration Date
Temperature	23.00 °C	23.00 °C	23.00 °C	2018-08-04 15:27:24
pH	7.77	7.77	7.77	2018-08-04 15:27:24
DO2	100.00 %	100.00 %	100.00 %	2018-08-04 15:27:24
Stirring Speed	100.00 %	100.00 %	100.00 %	2018-08-04 15:27:24
Air Flow	1.00 l/min	1.00 l/min	1.00 l/min	2018-08-04 15:27:24

Solaris controlling software offers a simply laid out, yet powerful platform for experimental design planning and process control. The graphical user interface enables the intuitive selection and adjustment of control functions.

Extracted data is compatible with Window Excel, but in addition, Solaris offers a platform where fermentation data can be easily exported in real time and thus managed. This software is included in the supply and can be installed on an unlimited number of the client's PC or laptops.

### Features:

- Home with Multi-level password protection
- Workflow settings (warm up, calibration, cultivation, cleaning, additional custom phases, etc.)
- Synoptic page with manual operation of all the actuators (pumps, valves etc.), parallel synoptic comparison between units
- Continuous trend graphs representation to track, print and export data on up to 6 processes and set point variables. Different dynamic zooms and configurations in a time frame that can be set interactively
- Cascade and profile programs
- Parallel set point settings



- Parallel Parameters Calibration (off and on line)
- Parallel trend comparison between parallel units
- Pumps configuration and calibration
- On line parameters calibration
- PID setting
- USB connection for free data extracting
- Remote control for after sale assistance; 100% assistance from our office
- Remote control for the user
- Possibility of saving up to recipes for repeat usage
- Print-out of hard copy of each screen
- Pumps Configurator