Sefia™ expansion system

CELL THERAPY MANUFACTURING

Sefia™ expansion system (Fig 1) comprises three hardware components: process unit, media storage unit and status indicator as well as dedicated application software and dedicated single-use kits to provide a comprehensive solution to your cell therapy manufacturing process. This automated and functionally closed system covers cell activation, transduction and expansion resulting in a standardized process for reliable autologous cell therapy manufacturing (Fig 2).

- **Streamlined manufacturing.** Using the same system via a single procedure to cover three consecutive steps of your manufacturing workflow.
- **Flexibility to meet your process needs.**Customizable parameters and specific kits enable the system to adapt to your individual process; accommodating all reagents and media.
- **Designed to increase productivity.** Reduce operator touchpoints and labor hours with high level of automation over three consecutive steps to help optimize your resources and costs.
- **Features designed to reduce batch failure risks.** Functionally closed single-use kit helps keep contaminants out. Control your process with real-time lab dashboards and alert notifications.
- **Easy integration.** User-friendly design of applications and consumables. Centralized data traceability, consistent setup duplication and regulatory compliance thanks to Chronicle™ software connectivity.

Fig 1. Sefia expansion system including process unit, media storage unit and status indicator.

Fig 2. General workflow for cell therapy manufacturing. The Sefia expansion system enables to perform the steps highlighted in green.

System overview

Hardware

The Sefia expansion system has been designed to support cell culture over three key steps of the cell therapy manufacturing workflow. The liquid (reagents, cell product, solutions, sampling) and sterile air transfers are supported via 2 peristaltic pumps, 16 pinch valves and 4 electro valves. Loadcells on hooks in the media storage and tilting platforms assure mass measurement over the process. The two tilting platforms also support the mixing of the culture vessel when required. The incubation of cells with any reagents is possible with temperature and CO_2 control thanks to two bottom heating plates (one per tilting platform), one top heater, an incubation temperature sensor and liquid temperature sensors as well as CO_2 controller and sensor. Two fans are also here to ensure the homogenization of air inside of the process drawer. In addition two sensors allow the pressure to be checked for the kit test and enable failure detection during the process. Finally, the connectivity and the status of the equipment are provided by two LED indicators and an LED beacon, one ethernet port and nine USB ports.

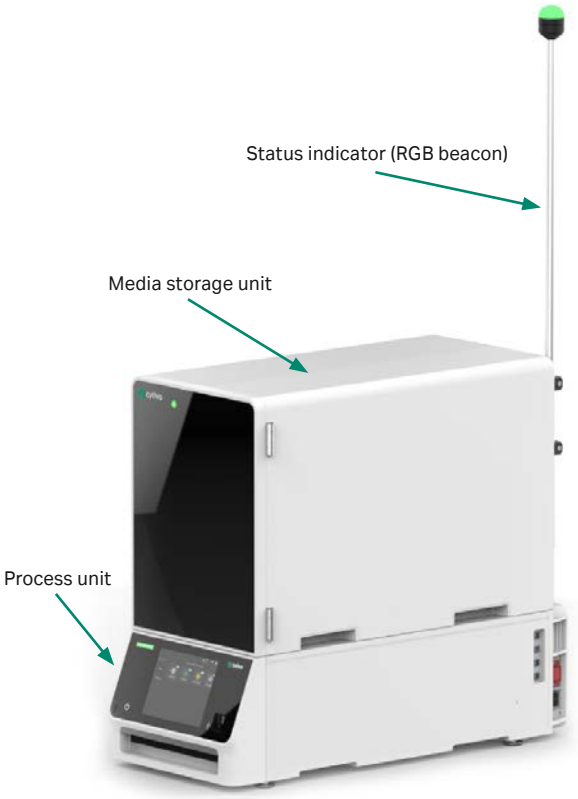

Fig 3a. Overview of Sefia expansion system components.

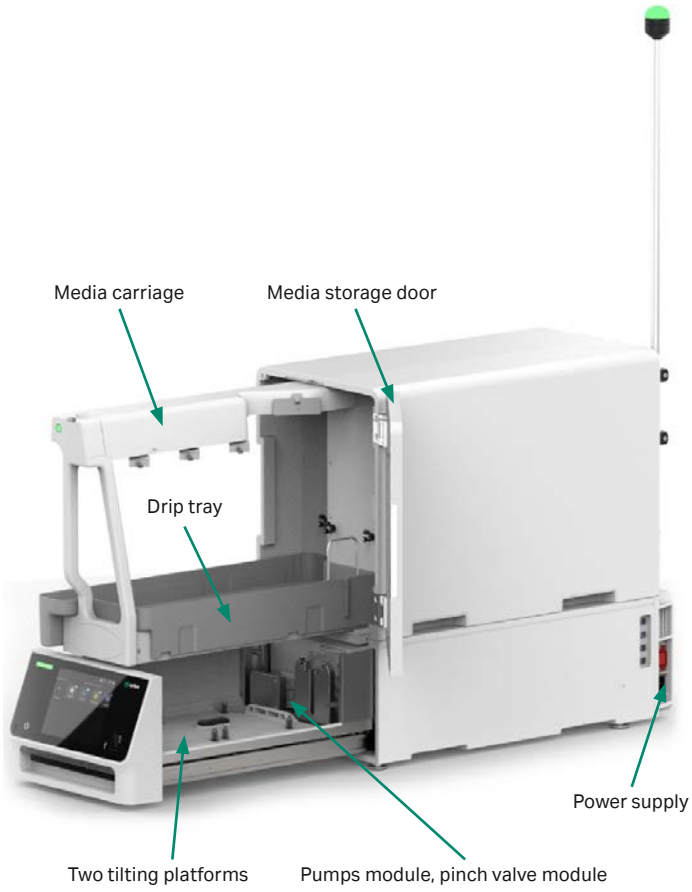

Fig 3b. Overview of Sefia expansion system components.

Software

All elements of the hardware are controlled by an embedded computer system with customized software for process automation accessed via a touchscreen user interface.

Universal application has been developed to cover the process steps required to activate the cell, transduce them with a viral vector, and finally expand cells to reach the target number.

Other applications have been developed to support additional needs such as troubleshooting.

Applications	Step	Single-use kit	Product
Universal	Activation, transduction and expansion	Sefia expansion kit	Biological application allowing for flexible setup and execution of activation, transduction and expansion steps.
Purge	Troubleshooting	Sefia expansion kit	Troubleshooting application allowing to evacuate cells from the culture vessel in case of failure conditions.
Disengage	Utility	N/A	Usability application allowing to disengage kit engagement mechanism outside of the biological application execution.
Diagnostic tool	Diagnostic	N/A	Application that allows user to automatically assess functionality of critical parts of the instrument. Application provides complete pass/fail report.

The Sefia expansion system can be connected to Chronicle automation software to monitor cell therapy manufacturing operation and supply chain logistics. Chronicle software enables the digitization of manufacturing documentation by generating electronic batch manufacturing records (eBMRs) through the use of electronic standard operating procedures (eSOPS). It also offers the ability to monitor instrument data in real-time and receive alert notifications via SMS and emails. Chronicle software centralizes the creation, approval, and deployment of parameter groups on connected Sefia expansion systems. Chronicle software supports cell therapy process development and manufacturing in compliance with FDA 21 CFR part 11 and EU Annex 11.

Consumables

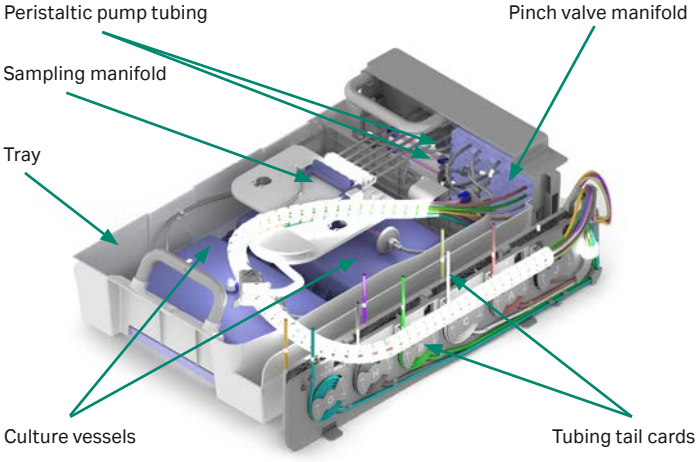

Fig 4. Sefia expansion single-use kit.

The Sefia expansion kit is a single-use kit for activation, transduction and expansion during CAR T cell therapy manufacturing processes. The kit is functionally closed, sterilized and contains two culture vessels as well as an array of tubing (Fig 4). The media and reagent lines of the kit are fitted to two tubing tail cards. The lines are color-coded to ease identification. The working mass of liquid is up to 628 g per vessel.

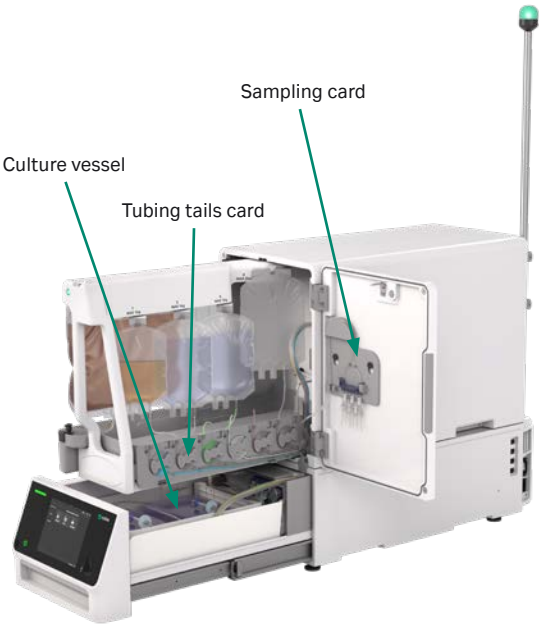

Fig 5. Sefia expansion kit installed on Sefia expansion system.

In addition, each Sefia expansion kit is equipped with an attached sample card (Fig 5). The sample card holds the sample manifold and six sample tails for collecting samples during a run.
All sample tails are equivalent, and their use should be managed by the user.

Sefia expansion kit is available in two types (FEP: fluorinated ethylene propylene and Si: silicone) to meet different customer needs. They both have the same volumes, the same architecture and are compatible with Universal application. The difference is the membrane material used for the culture vessels. In one of the kits, the membranes are FEP and in the other kit, they are silicone (Fig 6).

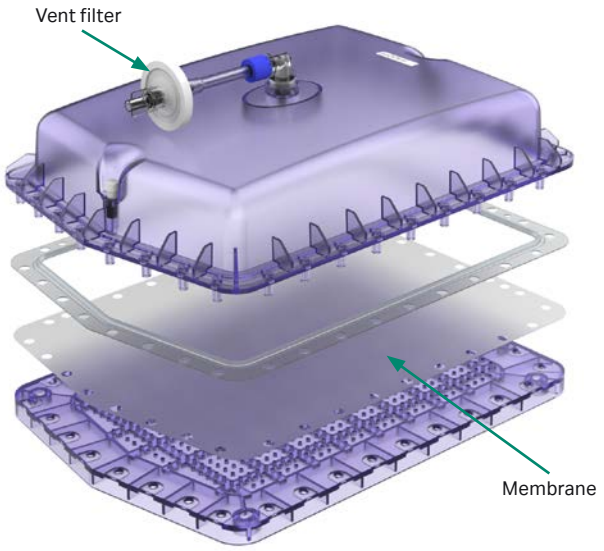

Fig 6. Detailed view of culture vessels including membrane and vent filter.

The vent filter is used during the kit test for pressure monitoring inside of the culture vessel and during the process for venting culture vessel to prevent excess pressure.

The membrane allows gas exchange between the culture and the external environment.

The four sterile air filters of each kit and the sterile air filter of the waste bag are integrity testable to help customers meet regulatory requirements. The test enables demonstration of the sterility of the filter and confirms that the filter has not been compromised during the procedure.

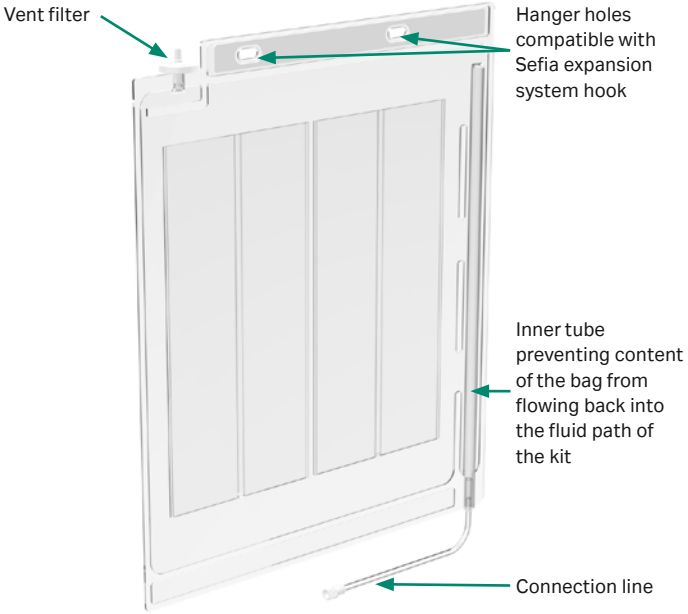

Fig 7. Sefia expansion waste bag.

The waste bag (Fig 7) is available as a standalone consumable of the Sefia expansion kit to be able to connect as many waste bags as required during your specific process.
It is recommended to use Sefia expansion waste bag when using Sefia expansion system.

Universal application overview

The Universal application covers three consecutive steps of your cell therapy manufacturing process: cell activation, transduction and expansion. You can start a procedure with Universal application with cellular product using a mass of between 5 and 250 g. Universal application default parameters are designed to execute one of many possible types of workflow, typically taking between 5 to 12 days. The cells are cultured in static culture vessels with temperature and CO_2 concentration control and monitoring. Sefia expansion system can be used with your current reagents and media. It has been tested with market-leading activators and media as well as various types of of viral vectors. Different methods can be used to support the cell expansion: batch, fed-batch or perfusion (Fig 8). At the end of the procedure, the genetically modified and expanded cells will be harvested in a bag up to 1200 g.

Key features of Universal application

Initial cellular product mass	5 to 250 g
Harvest bag	Up to 1200 g
Typical processing duration [1]	5 to 12 days
Supported expansion method	Batch Fed-batch Perfusion
Type of culture	Static
Control and monitoring	Temperature and CO_2 concentration

[1] For default parameters, may vary based on initial seeding cell number, used reagents and type of membrane used.

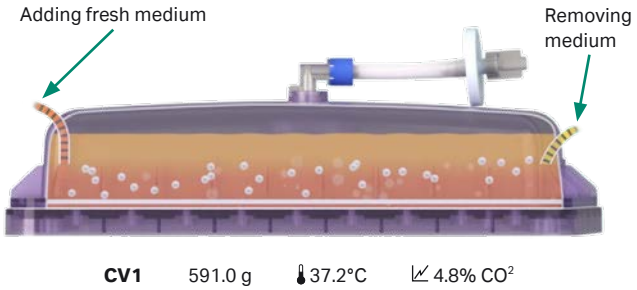

Fig 8. Illustration of cell expansion with perfusion method in Sefia expansion culture vessel.

Sefia expansion system Universal application offers high flexibility with customizable parameters that allow the operators to optimize activation, transduction and expansion steps.
For example, you can perform in parallel some activation steps and some transduction steps to optimize processing time (Fig 9).

You can also use the two culture vessels for the cell expansion by moving a portion of the cells from CV 1 to CV 2 and perform a parallel expansion step to optimize the final cell number (Fig 10).

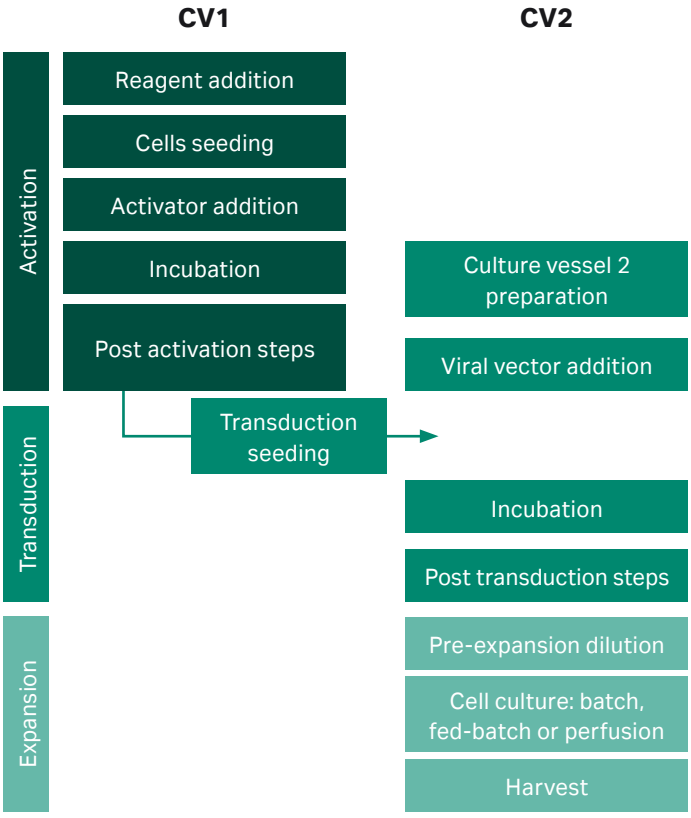

Fig 9. Example of workflow with parallel activation and transduction steps to optimize processing time.

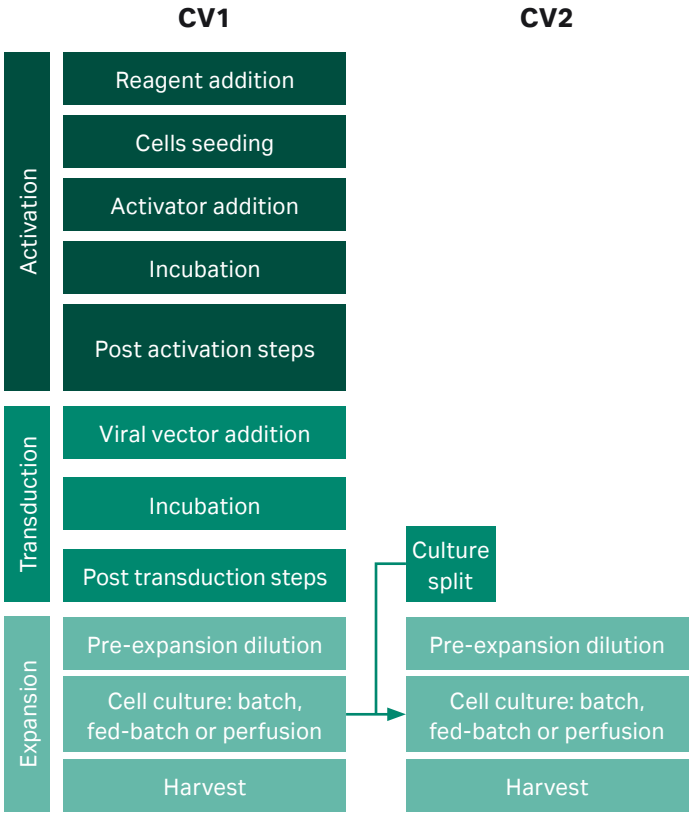

Fig 10. Example of workflow with parallel expansion step to optimize final cell number.

Performances

In the table below, of the performances obtained with the Sefia expansion system transduction efficiency at harvest over six experiments, three have been generated from fresh healthy donor apheresis and three from frozen healthy donor apheresis. Each apheresis has been processed using MagnetSelect application on Sefia Select system to isolated the T-cells. Then the isolated T-cells have been used as starting materials on Sefia expansion system to start the Universal procedure covering activation, transduction and cell expansion.

These performances are given for information as performance depends on parameter setting, used reagents and media as well as initial cellular product. The workflow can also be used for other types of viruses, activators and cell culture media.

Step	Description	Fresh healthy donor (n=3)	Frozen healthy donor (n=3)
Activation	Initial cellular product	Isolated T-cells from apheresis	Isolated T-cells from apheresis
	Activator	T Cell TransAct	T Cell TransAct
	Total viable cell seeding number for activation	100×10^6 in 150 mL suspension	100×10^6 in 150 mL suspension
	Activation marker expression post-activation	99.3%	84.2%
	Cell viability post-activation (day 5)	96.7%	95.2%
Transduction	Transduction efficiency at harvest	58.3%	52.2%
	Cell viability post-transduction	96.7%	95.2%
Expansion/general	Cell culture medium	Akron ImmunoCell Growth Medium (serum free)	Akron ImmunoCell Growth Medium (serum free)
	Average daily fold expansion	2.26	1.84
	Cell viability at harvest	98.1%	96.3%
	Cell recovery of cells from the culture vessel at time of harvest	96.0%	94.8%
	Number of cells at the end of the workflow	4.9×10^9 T-cells (day 8)	2.55×10^9 T cells (day 9)

Specifications

Hardware

Feature	Sefia expansion system
Dimensions (W × L × H) mm	System with RGB beacon: 380 × 886 × 1477 (adjustable to ± 150)
	System without RGB beacon: 380 × 886 × 768
Weight	Process unit: 42.2 kg
	Media storage unit: 38.8 kg
Power consumption	1000 W
Input voltage	100 to 240 VAC
Frequency	50/60 Hz
Core technology	Two tilting platforms
	2 peristatic pumps, 16 pinch valves and 4 electro valves
	Two pressure sensors
	Temperature and gas control
	Weight sensors on each hook and each tilting platform
	Culture volume range from 125 g to 1.2 kg (up to 628 g per vessel)
CO_2 connection	PMC 1603-3/16 hose barbed, non-valved connector
	Minimum: 1.2 bar and maximum: 5 bar
	288 L/day as maximum CO_2 consumption/leak rate
Connectivity	One ethernet port and nine USB ports
Software	Compatible with Sefia expansion applications only, Windows 10 and proprietary Sefia expansion software
User interface	Color touchscreen with an intuitive graphical user interface (GUI)
	Dynamic user guide to support operations
Traceability	Data management with PDF reports
User authentication	Role based configuration
	Authentication and permission using a customer's
	ActiveDirectory (AD) server
Electronic signature	Electronic signature is performed in Chronicle automation software only
Data exchange	Encrypted and secured
System log/audit trail	Every system action is recorded in the system log
	Data transfer populates associated equipment logs in Chronicle automation software

Consumables

Feature	Sefia expansion kits and waste bags
Shelf life	The kits have a shelf life of one year when stored at recommended storage temperature.
Sterility	Sterile by gamma irradiation, refer to the related validation guide for more information.
Materials in contact with cellular products	Polycarbonate (PC), fluorinated ethylene propylene (FEP), polypropylene (PP), polyvinyl chloride (PVC), silicone, and methylmethacrylate acrylonitrile butadiene styrene (MABS).
Lines	All the single-use kit line tails handled by the user as well as waste bag lines are compatible with sterile connection (SCD).
	Outer diameter (OD) is 4.1 mm and inner diameter (ID) is 2.6 mm for the weldable lines (PVC).

Safety and compliance

Sefia expansion system, combining a process unit and media storage unit, is a laboratory instrument with the CE mark (Machinery Directive 2006/42/EC). The system is intended for cell therapy manufacturing in good automated manufacturing practice (GAMP) compliant environments. The system is compliant with IEC-61010, IEC-61326, ICES-001 EMC requirement for Canada (Class A) and, China RoHS SJ/T11364-2014 standards.

Chronicle enables technical compatibility with ISPE GAMP 5, FDA 21 CFR Part 11 and EU GMP Annex 11 compliance.

Storage and operating requirements

Hardware

In addition to the environmental requirements outlined in the following table, installation of the Sefia expansion system must comply with the following general requirements:

- The room must have exhaust ventilation.
- The room must have forced ventilation for use of CO_2.
- The instrument should not be exposed to sources of heat, such as direct sunlight.
- Dust in the atmosphere should be kept to a minimum.
- The equipment must not be exposed to vibrations.

Parameter	Requirement
Allowed location	Indoor use only
Altitude, operating	Up to 2000 m
Ambient temperature, operating	15°C to 25°C
Ambient temperature, storage	0°C to 50°C
Atmospheric pressure, operating	840 to 1060 mbar
Pollution degree of the intended environment	Pollution degree 2
Relative humidity, operating	20% to 80%, non-condensing
Relative humidity, non-operating	20% to 80%, non-condensing

Consumables

The table below highlights the environmental requirements for storage and transport of Sefia expansion. Sefia expansion kits and waste bags must be stored in a clean and dry environment without chemical or biological contamination.

Mode	Storage
Temperature	+10°C to +30°C

Service information

OptiRun™ service solutions

Regulatory authorities require systems to be qualified and maintained within specifications during use in process scale-up and GMP-manufacturing. Our OptiRun™ service solutions offer a comprehensive range of services throughout the product's life cycle to support your technology, processes, and people.

Services	Product
Equipment installation	Installation can be performed by trained Cytiva service engineers
Preventive maintenance	Replacement of wear-and-tear parts and functional testing to ensure continuous performance of your instrument
Installation/ operational qualification (IQ/OQ) and re-qualification (RQ)	Standard and custom qualification services for Cytiva equipment throughpout its life cycle, including IQ/OQ, RQ, and continuous verification
Instrument upgrades	Hardware and software upgrades to keep your equipment state-of-the-art during its life cycle
Repairs	Field, remote and mail-in repairs are available depending on your instrument type and environment
Digital services	A range of digital solutions, from remote assistance to network installation and virtual support and trainings
Spare parts	High quality spare parts for use in GxP environment; parts security of supply consultancy
Relocation support	Preparing your equipment to be moved and re-installed in its new location
Service plans	A range of plans to support your operations and instrument performance

Ordering information

Products	Product code
Sefia expansion system package (including process unit, media storage unit and status indicator)	29746257
Sefia expansion media storage unit	29722941
Sefia expansion system (process unit)	29413640
Sefia expansion status indicator (RGB Beacon)	29722942
Sefia expansion kit - FEP	29716713
Sefia expansion kit - silicone	29739346
Sefia expansion waste bag (10 pack)	29732203

Related products	Product code
Chronicle software Pre-GMP base annual subscription	29734890
Chronicle software GMP base annual subscription	29734894
eBinder IQ/OQ Sefia expansion system	29745977

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