

	USER REQUIREMENT SPECIFICATION	Document number 01/2025	
		Version No.:	01.00
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		Effective date:	14.11.2025

**USER REQUIREMENT SPECIFICATION OF FILL/FINISH MACHINE
INSTALLED WITHIN RESTRICTED ACCESS BARRIER SYSTEM**






Final approval of the User Requirements Specification			
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1. INTRODUCTION

Bioceltix SA intends to install a new automatic fill/finish machine intalled within restricted access barrier system in Production Facility located in Bioceltix S. A., Ideal Idea hall, ul. Skrzypowa (dawniej jako ul. Brzezińskiego), 54-530 Wrocław, Polska.

This specification defines the User Requirements for the new fill/finish machine intalled within restricted access barrier system and it will also be used as a basis for qualification.

This URS will serve as a technical document for a SUPPLIER selection, purchase order and qualification practices.

1.1. Document applicability

This document will be as part of the validation documentation for the new fill/finish machine intalled within restricted access barrier system

1.2. Document contractual status

Qualification Protocols and reports for FAT/SAT/DQ/IQ/OQ should be developed and executed by the vendor/supplier. All these protocols/reports should be approved by *Bioceltix SA*, before and after qualification.

2. OVERVIEW

2.1. Design of Fill/Finish machine installed within restricted access barrier system

The design and construction of the fill/finish machine intalled within restricted access barrier system control shall be in accordance with a current industry interpretation of EU Good Manufacturing Practice Volume 4 – GMP Guidelines, Part 1: Chapter 3 (Premises and Equipment), Chapter 5 (Production), Chapter 6 (Quality Control), EU GMP Volume 4 – GMP Guidelines, Annex: Annex 1 (Manufacture of Sterile Medicinal Products), Annex 11 (Computerised Systems) and FDA requirements mentioned in 21 CFR Part 11, 21 CFR Part 210 as applicable to this type of equipment.

2.2. Equipment/System owner

The primary owner of the fill/finish machine intalled within restricted access barrier system will be Manufacturing Unit.

2.3. Key objectives and benefits (intended use)

The objective of this User Requirement Specification (URS) is to describe requirements regarding a fill/finish machine intalled within restricted access barrier system.

2.4. Main system/equipment functions

Fill/finish machine intalled within restricted access barrier system will be used for aseptically filling of pharmaceutical products (stem cell suspension), ensuring sterility, precision and compliance with regulatory standards. The URS include process and technical aspects for the equipment. This URS does not cover financial or legal aspects concerning the purchasing process.

3. REQUIREMENTS

The operational, system functions, data and interface requirements are specifically detailed in the following Requirements matrixes. Requirements designation is as follows:

- The mandatory requirements are designated "M".
- The optional requirements are designated "O".

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3.1. Requirements matrix for fill/finish machine installed within restricted access barrier system

No.	Description	Priority	Assessment Yes/ No/ N/A
3.1.1. Hardware			
URS-3.1.1.01	PLC-based control system with HMI touch-screen interface, where all monitored parameters are displayed.	M	
URS-3.1.1.02	The System halt should be provided in case of system failure or safety issue.	M	
URS-3.1.1.03	The System should be connected to Bioceltix network and time synchronized	M	
URS-3.1.1.04	Operator station (HMI) should provide control, visualization and supervision of process parameters (synoptic screens) with actual parameters function, with alarm functions (on screen) and alarms acknowledgement.	M	
URS-3.1.1.05	The input of parameters by the user should be simple and clear. A freely adjustable limitation of the parameter input (min / max) must be possible. The meaning of the parameter must be obvious and not misleading. It must be possible to confirm critical inputs (user and password).	M	
URS-3.1.1.06	Operator station (HMI) should be in Polish and English languages.	M	
URS-3.1.1.07	Interface for volume and filling parameters control.	M	
URS-3.1.1.08	Numeric and/or graphical process parameters data display.	M	
URS-3.1.1.09	Communication interface: Ethernet port for communication with computer.	O	
URS-3.1.1.10	Computer for process data collection.	O	
URS-3.1.1.11	Remote monitoring capability.	O	
URS-3.1.1.12	SCADA integration for data logging, batch records, and reporting.	M	
URS-3.1.1.13	Particule Monitoring System shall be integrated to EMS.	M	
3.1.2. Software			
URS-3.1.2.01	Process parameters registration software.	M	
URS-3.1.2.02	Software must be controlled by active directory users.	M	
URS-3.1.2.03	Software must be compliant with 21 CFR Part 11.	M	
3.1.3. Alarms			
URS-3.1.3.01	Low or high filling volume beyond acceptable limits.	M	
URS-3.1.3.02	Power failure or sudden shutdown.	M	
URS-3.1.3.03	Abnormal pressure or vaccum conditions within RABS.	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
URS-3.1.3.04	Deviation in HEPA airflow velocity or integrity failure.	M	
URS-3.1.3.05	Pump failure or tubing blockage affecting liquid transfer.	M	
3.1.4. Data management			
URS-3.1.4.01	The system should allow the export of e-records in portable format (e.g., XLS, PDF).	M	
URS-3.1.4.02	If the retention strategy is not able to keep e-records in the original system, the computer system (CS) should have implemented a mechanism for archiving e-records in a standard format file (eg PDF, Common / global XML Standards). The chosen format can be replaced by the most modern technology.	M	
URS-3.1.4.03	Procedure for data Archiving should be available.	M	
URS-3.1.4.04	There must be a possibility to create and store batch data records (reports). Each run / test data will be collected, electronically recorded and archived in portable format (e.g. pdf).	M	
URS-3.1.4.05	<p>The SCADA system shall be capable of generating a Batch Report containing at minimum the following information, in accordance with Good Automated Manufacturing Practice (GAMP) and 21 CFR Part 11 requirements:</p> <ul style="list-style-type: none"> • Batch start date and time; • Batch end date and time; • Batch description (name, batch number); • Logged-in user ID initiating the batch; • Total number of good vials produced; • Total number of rejected vials; • Individual weight of each vial (both accepted and rejected); • Weight trend of vials throughout the batch; • Date and time of each alarm occurrence; • Date and time of each alarm acknowledgment/reset; • Unique alarm identifier (Alarm ID); • User ID of the operator who performed the electronic signature for each alarm requiring such authorization. 	M	
3.1.5. Data security			
URS-3.1.5.01	All historical records should be available to print.	M	
3.1.6. Access to the system			
URS-3.1.6.01	<p>The access rights for the software must be managed by at least the following user groups:</p> <ul style="list-style-type: none"> • Operator; • Supervisor; 	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
	<ul style="list-style-type: none"> Maintenance; Administrator. 		
URS-3.1.6.02	<p>The system should allow quality passwords, e.g. Numbers and letter complexes. The current ISEC rule requires passwords consisting of at least 8 characters and containing 3 of the following 4 elements:</p> <ul style="list-style-type: none"> At least 1 uppercase letter; At least 1 lowercase letter; At least 1 number; At least 1 special character. 	M	
URS-3.1.6.03	The system must have a mechanism that automatically locks access if it has not been serviced for 15 minutes.	M	
3.1.7. Audit of user actions			
URS-3.1.7.01	The system automatically generates an audit trail for user actions.	M	
URS-3.1.7.02	<p>Computer-generated audit trails should include:</p> <ul style="list-style-type: none"> User ID of the person who performs the action (WHO); Date and time of execution (WHEN); Which parameter has been changed and from and to which value (WHAT); Possibly reason for action (WHY). 	M	
URS-3.1.7.03	The audit trail can neither be modified nor deleted or deactivated by users with a general access authorization.	M	
URS-3.1.7.04	The audit trail must be accessible for verifications and printouts.	M	
3.1.8. User interface			
URS-3.1.8.01	Numeric and/or graphical process parameters data display for viewing and set parameters of equipment.	M	
3.1.9. Supplier Documentation and Qualification requirements			
URS-3.1.9.01	SUPPLIER must deliver following documents according to agreed timeline from kick-off meeting:	M	
URS-3.1.9.02	Completed User Requirements Specification matrix with all deviations	M	
URS-3.1.9.03	List of major components (incl. dimensions and main technical parameters).	M	
URS-3.1.9.04	Equipment and Instrument List	M	
URS-3.1.9.05	Datasheets of all Instruments and Equipment	M	
URS-3.1.9.06	P&ID	M	
URS-3.1.9.07	Layout	M	
URS-3.1.9.08	Alarm List for GMP Alarms	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
URS-3.1.9.09	User and Maintenance manual and ancillary equipment e.g. PMS, Microbial Air Sampler, glove tester.	M	
URS-3.1.9.10	User and Maintenance manual in English and Polish.	M	
URS-3.1.9.11	Cleaning instruction.	M	
URS-3.1.9.12	Control system manual (description, installation, maintenance, wiring diagram)	M	
URS-3.1.9.13	List of recommended spare parts, wearing parts with name of SUPPLIER and SUPPLIER article no.	M	
URS-3.1.9.14	Utility consumption and connection specification	M	
URS-3.1.9.15	Electric schematics	M	
URS-3.1.9.16	Pneumatic Schematics	M	
URS-3.1.9.17	Noise generation data	M	
URS-3.1.9.18	Material certificates (for product contact and primary packaging parts)	M	
URS-3.1.9.19	Report from roughness test (for product contact and primary packaging parts)	M	
URS-3.1.9.20	The machines measuring instruments calibration procedures and calibration certificates	M	
URS-3.1.9.21	Certificates of instruments and materials (e.g. Gloves, HEPA Filters used during FAT / SAT testing) used during qualification tests	M	
URS-3.1.9.22	Calibration certificates of calibration equipment.	M	
URS-3.1.9.23	Sealing materials FDA compliance certification (for product contact and primary packaging parts)	M	
URS-3.1.9.24	I/O List	M	
URS-3.1.9.25	Trouble shooting guide.	M	
URS-3.1.9.26	Functional Design Specification (FDS)	M	
URS-3.1.9.27	Hardware Design Specification (HDS)	M	
URS-3.1.9.28	Software Design Specification (SDS)	M	
URS-3.1.9.29	Software Validation Certificate	M	
URS-3.1.9.30	Back up (Disaster recovery)	M	
URS-3.1.9.31	Software licenses (including conformity to 21 CFR PART 11, as per SUPPLIERS statement)	M	
URS-3.1.9.32	FAT Protocol	M	
URS-3.1.9.33	Risk Analysis	M	
URS-3.1.9.34	Design Qualification with Protocol and Report	M	
URS-3.1.9.35	Installation Qualification Protocol / SAT	M	
URS-3.1.9.36	Installation Qualification Report	M	
URS-3.1.9.37	Operational Qualification Protocol	M	
URS-3.1.9.38	Operational Qualification Report	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
URS-3.1.9.39	Quality Plan delivered by supplier should cover at least: <ul style="list-style-type: none"> Brief description of QMS; Tasks and responsibilities; Validation policy; Documentation management; Change management; Deviation management; Deliverables. 	M	
URS-3.1.9.40	Declaration of conformity for all applicable CE marking directives.	M	
URS-3.1.9.41	Documents should be delivered in one paper (with date and signature) and one electronic copy.	M	
URS-3.1.9.42	Valid offer with description of equipment	M	
Factory Acceptance Test – FAT			
URS-3.1.9.43	The FAT will follow the <ul style="list-style-type: none"> The aim of FAT is work inspection and functional tests of constructed equipment. SUPPLIER will prepare a Test Plan which must include detailed list of FAT tests. Work inspection and functional tests of constructed equipment (Factory Acceptance Test – FAT) will be carried out at SUPPLIER's premises by SUPPLIER and CLIENT's representatives. SUPPLIER shall be responsible for executing the FAT according to the schedule. During FAT not only capacity of the line will be taken into consideration, but also quality of filling operation. 	M	
URS-3.1.9.44	SUPPLIER shall also produce the report upon completion of FAT and shall commit to resolve any deviations identified during the FAT execution. FAT positive completion is a condition to release shipment.	M	
URS-3.1.9.45	SUPPLIER shall propose a Test Plan, which will be verified (modified if necessary) and approved by CLIENT, and will be resubmitted to SUPPLIER prior to FAT execution.	M	
URS-3.1.9.46	Any costs, which are caused by a prolongation of FAT due to the failure of test(s) shall be covered by SUPPLIER.	M	
URS-3.1.9.47	A detailed list of all FAT tests will be approved as part of the FAT Plan. At least a one-hour run for 4R should be performed.	M	
URS-3.1.9.48	All control switches, alarms, safety interlocks, and all instruments shall be checked prior to test and	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
	during testing. Instruments shall be calibrated before testing.		
URS-3.1.9.49	SUPPLIER shall also produce the report upon completion of FAT and shall commit to resolve any deviations identified during the FAT execution. FAT positive completion is a condition to release shipment	M	
Site Acceptance Test – SAT			
URS-3.1.9.50	An on-site acceptance tests (SAT) shall be performed by SUPPLIER at CLIENT's site witnessed by the CLIENT's representatives. A test run must be executed for at least 2 hrs for 4R (vials), details of run and acceptance criteria to be included in test plan.	M	
URS-3.1.9.51	SUPPLIER shall propose a Test Plan, which will be verified (modified if necessary) and approved by CLIENT, and will be resubmitted to SUPPLIER prior to SAT execution.	M	
URS-3.1.9.52	SUPPLIER shall be responsible for executing the SAT according to the schedule. Any costs, which are caused by a prolongation of SAT due to the failure of test(s) shall be covered by SUPPLIER.	M	
URS-3.1.9.53	As general rule, the functional tests done during FAT execution should be repeated. Detailed list of all SAT tests will be approved as a part of SAT Plan	M	
URS-3.1.9.54	During the SAT/Start-up phase, critical instruments must be in initial period of calibration validity.	M	
URS-3.1.9.55	Operation of equipment during SAT/Start-up shall be done by SUPPLIER and is a part of Scope of Supply.	M	
URS-3.1.9.56	SUPPLIER shall also produce the report upon completion of SAT and shall commit to resolve any deviations identified during the SAT execution. Any changes required to meet the specification shall be implemented, recorded and all documentation shall be up-dated and resubmitted to the CLIENT at no cost to the CLIENT.	M	
URS-3.1.9.57	SAT positive completion is a condition to release Installation and Operational Qualification (IQ/OQ). Note: Similar documentation should be provided for ancillary equipment if provided e.g. for PMS, Microbial Air Sampler and Gloves Integrity tester	M	
Design Qualification – DQ			

No.	Description	Priority	Assessment Yes/ No/ N/A
URS-3.1.9.58	Design Qualification will be carried out by SUPPLIER. SUPPLIER shall deliver all required for this purpose documents approved by the CLIENT	M	
URS-3.1.9.59	To identify the critical components of system/equipment the Component Criticality Assessment (CCA) shall be performed by SUPPLIER and approved by CLIENT. On the base of approved CCA, SUPPLIER will perform the Risk Analysis (RA).	M	
URS-3.1.9.60	Risk Analysis should identify the level of risk associated with each component and functions of device/ system, and should be the basis for the scope of qualification tests. Both CCA and RA activities shall be done before DQ during designing phase.	M	
URS-3.1.9.61	SUPPLIER should prepare DQ qualification, which demonstrates that the device meets the GMP requirement and user requirements (URS), based on the own documentation. Next qualification should be accepted by CLIENT. DQ report should be available during FAT tests.	M	
Installation Qualification Test – IQ			
URS-3.1.9.62	SUPPLIER is responsible for execution of the Installation Qualification (IQ) under supervision of CLIENT.	M	
URS-3.1.9.63	<p>There is a requirement to complete qualification which will be based on Functional Risk Analysis, but should cover at least:</p> <ul style="list-style-type: none"> As-built documentation verification (e.g. P&ID, layouts, etc.) Technical documentation verification (e.g. data sheets, declarations, licences, technical specifications, required for IQ / OQ) Drawing, Lists and P&ID walk-down Utilities verification Critical instrument manufacturer's calibration certificates verification Testing equipment calibration verification Verification of correctness of installation vs approved documentation. <p>For computerised system:</p> <ul style="list-style-type: none"> As-built documentation verification (Functional Specification, Design and Configuration Specification, HDS/SDS) Hardware/Software Installation Verification 	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
	<ul style="list-style-type: none"> Visualization verification (HMI / SCADA) Input/Output Verification CFR 21 Part 11 and Annex 11 to GMP compliance verification Power supply test Alarm Verification Access Level Control / Security Verification Audit Trail Testing Back-Up and Recovery Procedure Verification HMI/Screen Functionality Verification Reporting (including printouts) Archiving / Trending Data security Power failure test / Emergency stop test. 		
URS-3.1.9.64	In case of failure, tests will be repeated by SUPPLIER and any costs, which are caused by a prolongation of IQ shall be covered by SUPPLIER.	M	
URS-3.1.9.65	SUPPLIER will also create the IQ-Report upon completion of IQ, accepted by CLIENT, with the information that OQ qualification could start and shall commit to resolve any deviations identified during the IQ execution.	M	
URS-3.1.9.66	IQ positive completion is the condition to release for Operational Qualification (OQ).	M	
Operational Qualification Test – OQ			
URS-3.1.9.67	SUPPLIER is responsible for execution of Operation Qualification (OQ) under supervision of CLIENT.	M	
URS-3.1.9.68	SUPPLIER shall present a concept of OQ Plan which will be verified (modified if necessary) and approved by CLIENT prior to OQ execution. IQ and OQ tests should be based on risk analysis (functional risk assessment) SUPPLIER shall be responsible for executing the OQ according to the schedule.	M	
URS-3.1.9.69	In case of failure, tests will be repeated by SUPPLIER and any costs which are caused by a prolongation of OQ shall be covered by SUPPLIER.	M	
URS-3.1.9.70	Operation of equipment during OQ shall be done by SUPPLIER and is a part of SCOPE OF SUPPLY.	M	
URS-3.1.9.71	All necessary raw and auxiliary materials will be supplied by CLIENT.	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
URS-3.1.9.72	SUPPLIER is responsible for execution of IQ/OQ for PMS, Glove Integrity Tester and Microbial Air Sampler under supervision of CLIENT.	M	
URS-3.1.9.73	The SUPPLIER will provide training adequate for: operator, maintenance for Bioceltix's employees. The training will instruct the operating personnel in the proper operation of the equipment and the technical staff introduce to the maintenance, adjustment, calibration of instruments, and troubleshooting / repair of equipment.	M	
3.1.10. Regulations and standards			
URS-3.1.10.01	Basic Requirements for Medicinal Products: <ul style="list-style-type: none"> EU GMP Volume 4 - GMP Guidelines, Part 1: Chapter 3 (Premises and equipment) Chapter 5 (Production) Chapter 6 (Quality Control) EU GMP Volume 4 - GMP Guidelines, Annex: Annex 1 (Manufacture of Sterile Medicinal Products) Annex 2 (Manufacture of biological medicinal products for human use) 	M	
URS-3.1.10.02	FDA GMP 21 CFR Parts 11, 210, 211 and part 600	M	
URS-3.1.10.03	CE conformity: In accordance with European Union directives.	M	
URS-3.1.10.04	ISPE Baseline Pharmaceutical Engineering Guides: <ul style="list-style-type: none"> Volume 3 (Sterile Manufacturing Facilities), Volume 6 (Biopharmaceutical Manufacturing Facilities). 	M	
3.1.11. Technical design			
URS-3.1.11.01	The system is to be designed for the filling, stoppering and capping of pre-sterilized vials, which must fit inside the facility layout (refer to attachment 01)	M	
URS-3.1.11.02	Design and construction shall be in accordance with SUPPLIER's proven standards for the pharmaceutical industry conditions and shall incorporate the design features and material requirements indicated herein.	M	
URS-3.1.11.03	The Filling line should work as a fully automated machine, which should fit into room layout see attachment 01.	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
URS-3.1.11.04	The machine will be served as following functions: <ul style="list-style-type: none"> • De-Bagging of tubs and conveying tubs into Sterile Area. • NTT and De-Lidding of pre-sterilized units (vials) • Filling (vials) • Pre and Post weighing capable of performing 0-100 % IPC • Closing (stoppering and crimping) • Particle Monitoring System • Microbial Air Sampler – volumetric method • Gloves Integrity Tester • Outfeed conveyor belt from the machine, through the wall of the cleanroom for further processing. 	M	
URS-3.1.11.05	There should be no glass-to-glass contact, or, should be minimized as much as possible.	M	
URS-3.1.11.06	Glass damages and glass defects during transport through the whole line must be avoided. There is a requirement to ensure that during production fallen or broken vials is kept to below 0.1% Providing packaging material are without damage.	M	
URS-3.1.11.07	Possibility to fill different products should be considered. The adapted technology should give maximum flexibility and minimize the risk of cross-contamination between different products.	M	
URS-3.1.11.08	Fast and simple format size change parts with little or no need for use of tools during assembly / disassemble	M	
URS-3.1.11.09	Accessibility of all areas that require regular cleaning, operating, service or maintenance work.	M	
URS-3.1.11.10	Physical barrier for complete line Open RABS or other appropriate measures are required to ensure aseptic production without contamination. The physical barrier (Open RABS) have to consist of:	M	
URS-3.1.11.11	The whole process to be visible through the Open RABS's windows / doors	M	
URS-3.1.11.12	The Open RABS should have an adequate number of doors that allow performing operations associated with the process, format change, qualification, cleaning and maintenance, including easy access for filter change-out.	M	
URS-3.1.11.13	The oRABS doors have to be supplied with interlock and alarm system, including a safety light beam for the control of entry by the Operator into the oRABS unit through gloves.	M	
URS-3.1.11.14	The oRABS should be able to have installed (gloves single / double layered) enabling access to any area within the equipment.	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
URS-3.1.11.15	The layout of the equipment within the unit should allow for adequate space for storage of consumables such as settle plates, Lint free wipes, designated tools etc. Or alternative system be designed	M	
URS-3.1.11.16	There is a requirement for the debagging process to be performed under a LAF unit, ensuring no contamination will be transferred into the filling area from this process	M	
URS-3.1.11.17	The first bag removal shall be performed using gloves.	M	
URS-3.1.11.18	The debagging unit will be installed in the vial processing room (Grade D).	M	
URS-3.1.11.19	The machine will be installed in filling room (Grade B) Environment conditions: <ul style="list-style-type: none"> Temperature: 19°C ± 2°C Humidity: 30 ÷ 60% Air changes min.: 44 	M	
URS-3.1.11.20	The NTT and De-lidding will be performed inside the LAF (zone A)	M	
URS-3.1.11.21	The Filling and stoppering area has to be inside the LAF (zone A); protected unit has to be separated from the capping step to avoid the contamination of product with particles.	M	
URS-3.1.11.22	The Capping of vials will be performed inside the LAF (zone A)	M	
URS-3.1.11.23	The air flow between the different zones must be controlled to ensure the product is protected within the different zones	M	
URS-3.1.11.24	LAF speed 0,45 +/- 20 % must be delivered at working height (there should be continuous measurement / control of the speed)	M	
URS-3.1.11.25	There should be a measurement across the HEPA filters showing any drop in pressure	M	
URS-3.1.11.26	Under LAF will be located sterile zone – class A, ISO 5 environment.	M	
URS-3.1.11.27	Max content of impurities (non-viable particles) in 1 m ³ indicated below (EU GMP Annex 1 and EN ISO 14644-1): Class A: (at rest and in operation) ≥ 0.5 µm maximum 3520 particles, ≥ 5.0 µm maximum 20 particles	M	
URS-3.1.11.28	Max content of impurities (viable particles): - Active air sampling: no growth	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
	- Passive air sampling: no growth (sedimentation plate diameter 90 mm) - Surfaces: no growth (plate diameter 55mm).		
URS-3.1.11.29	Inside of LAF there is a need for permanent particle monitoring and LAF parameters at critical points. Sampling point for particle monitoring and air sampling, numbers of probes and locations will be determined after Risk Analysis completed and verified after Mock Up visit.	M	
URS-3.1.11.30	Filters: Pre-Filter: Fine dust filter Main Filter: Particles filter, HEPA filter, filter class H14 according to EN1822, filtration efficiency of 99.995 %. The LAF air intake should be taken from the LAF top.	M	
URS-3.1.11.31	Main filter integrity – The laminar flow is equipped with Tri-Clamp connection for aerosol tests.	M	
URS-3.1.11.32	The integrity test of the gloves should be carried out under LAF (Class A).	M	
URS-3.1.11.33	Stoppers should be transferred to the stopper bowl via an RTP port. Opening of the port should be performed using gloves from Class A (under LAF).	M	
URS-3.1.11.34	Filp off Caps should be transferred to the cap bowl via an RTP port. Opening the port should be performer using gloves from Class A (under LAF).	M	
URS-3.1.11.35	The primary packaging materials will be delivered to the facility as follow: <ul style="list-style-type: none"> Vials – pyrogen-free and pre-sterilized (RTU) Stoppers – pyrogen-free and ready to sterilize (RTS) or pre-sterilized (RTU) Filp off Caps – ready to sterilize caps (RTS) or pre-sterilized (RTU) 	M	
URS-3.1.11.36	Format part changes or assembly/disassembly should be performed with minimal risk of particle generation.	M	
Filling Vials:			
URS-3.1.11.37	The debuggng will be fed manually – system for transferring nested ready to use containers to the machine in aseptic condition should be designed and adopted.	M	
URS-3.1.11.38	The design of filling station should limit the impact with the unidirectional air flow in order to avoid turbulence during the filling operation.	M	
URS-3.1.11.39	Peristaltic pump to guarantee small filling volume accuracy over entire filling process. The pump should meet Client's preferences and standards.	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
	This pump should be recommended and supplied by SUPPLIER.		
URS-3.1.11.40	All non-SU equipment which gets in contact with the product must be able to be sterilized by autoclaving.	M	
Stoppering and Crimping Vials			
URS-3.1.11.41	An automated closing station for vials stoppering and sealing operations must be delivered.	M	
URS-3.1.11.42	During the stoppering and crimping process the creation of particles should be minimized.	M	
URS-3.1.11.43	Automatic rejection system – Incomplete vials (without stopper or cap) are automatically rejected on a reject outfeed rail. These should be logged and tracked by ‘Shift Register’ for correct reject verification. Separate sensor to confirm rejection. All rejected containers must be collected in a reject bin designed to prevent spillage of product, or containment of product in bin if any spillage occurs.	M	
URS-3.1.11.44	Splitting the conveyor belt to avoid any risk of cross-contamination from Grade D to Grade B.	M	
URS-3.1.11.45	The machine shall be equipped with an additional manual lifting system at the outfeed for transferring sets/trays of filled vials within the filling room (Grade B), to be used in the event of an outfeed conveyor belt failure.	M	
URS-3.1.11.46	SUPPLIER provide an accurate requirement for the media (utilities) and the specification of connection.	M	
URS-3.1.11.47	Connecting the machine to the media (utilities) will be held under the supervision of the SUPPLIER.	M	
URS-3.1.11.48	The system must be made of materials, metallic and non-metallic, such as to minimize the risks of particulate loss in the product and in the room in which it is installed.	M	
URS-3.1.11.49	All components which have direct contact with product or primary packaging materials are made of stainless-steel AISI 316L.	M	
URS-3.1.11.50	For steel parts not contacting with product, located in pharmaceutical room (external elements, support structures etc.) AISI 304L or adequate is allowed; matt finished required all other non-steel materials shall be SUPPLIER's standard.	M	
URS-3.1.11.51	Roughness of product / primary packaging material contact surfaces $R_a \leq 0.6$, electro polished.	M	
URS-3.1.11.52	Roughness coefficient of external surface $R_a \leq 1,6 \mu\text{m}$, electro polished.	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
URS-3.1.11.53	Gaskets, sealing and lubricants (H1) approved for use in pharmaceutical production for product contact parts accompanied by a FDA certification is required.	M	
URS-3.1.11.54	The non-metallic material must be capable of withstanding the operating temperature of the system as well as solvents, detergents and disinfection agents normally used in the production cycle.	M	
URS-3.1.11.55	For all material used in machine construction material and hygienic certificates have to be delivered and included to documentation for product contact parts and primary packaging materials.	M	
URS-3.1.11.56	All components of metal material must be accompanied by a certificate for product contact parts and primary packaging materials which guarantees the traceability.	M	
URS-3.1.11.57	All used plastic / thermoplastic materials must be accompanied by a certificate attesting compliance with FDA 21 CFR.177 requirements for product contact parts and primary packaging material.	M	
URS-3.1.11.58	All applied materials may not shed particles or fibers, which could contaminate the product.	M	
URS-3.1.11.59	Power supply: 200–240VAC 50/60Hz + PE max 20 AMP	M	
URS-3.1.11.60	Container compatibility – plastic and glass vials.	M	
URS-3.1.11.61	No vial – no fill sensor	M	
URS-3.1.11.62	The filling machine must operate within a closed RABS environment.	M	
URS-3.1.11.63	CIP/SIP(Clean-in-Place/Sterilize-in-Place) capability preferred.	O	
URS-3.1.11.64	Equipped with HEPA filtration (Grade A unidirectional airflow)	M	
URS-3.1.11.65	Non-destructive in-process statistical weight verification for dose accuracy.	M	
URS-3.1.11.66	Linear vials flow	M	
3.1.12. Supply listing			
URS-3.1.12.01	Warranty: at least 2 years.	M	
URS-3.1.12.02	Supply of spare parts (parts produced by vendor) must be guaranteed for at least 7 years after the installation of the equipment.	M	
URS-3.1.12.03	Technical support from supplier, if fill/finish machine intalled within restricted access barrier system or its parts are damaged, must be provided during 48 hours.	M	

No.	Description	Priority	Assessment Yes/ No/ N/A
URS-3.1.12.04	In case of malfunction the Supplier must provide technical advice and help for the warranty period and after.	M	
3.1.13. Performance requirements			
URS-3.1.13.01	The filling machine will dispense the stem cell suspension, delivered in SU bags, into 2R vials.	M	
URS-3.1.13.02	The initial batch size will be 1000 vials, with a target of 3000 vials.	M	
URS-3.1.13.03	It must be capable of filling 1.11 ml with product volumes ranging from 1.10 to 1.12 ml. The filling and stoppering section must have a minimum of 2 stations.	M	
URS-3.1.13.04	Filling accuracy $\pm 1\%$	M	
URS-3.1.13.05	Installed pump type – peristaltic pump with single-use tubing.	M	
URS-3.1.13.06	Single-use assemblies (tubing and nozzles) will be used during the filling process.	M	
URS-3.1.13.07	Filling line must be equipped with a recirculation system to prevent sedimentation of the suspension	M	
URS-3.1.13.08	Vial size: 2R. Glass and plastic vials.	M	
URS-3.1.13.09	The filling line must be designed to allow future compatibility with 4R up to 10R vials.	O	
URS-3.1.13.10	Production capacity minimum 50 units per minute	M	

4. CALCULATIONS AND ALGORITHMS

4.1. Calculations		
URS-4.1.01	N/A	N/A
4.2. Algorithms		
URS-4.2.01	N/A	N/A

5. DEFINITIONS AND ABBREVIATIONS

$^{\circ}\text{C}$ – degree Celsius
 CE- European Conformity
 DQ – Design Qualification
 EU – European Union
 EMS – Environmental Monitoring System
 FDA – Food and Drug Administration
 FAT – Factor Acceptance Test
 GMP – Good Manufacturing Practice
 GIT – Glove Integrity Tester
 Hz – Hertz
 HMI – Human Machine Interface
 IQ – Installation Qualification
 K - Kelvin

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L – Litre
 Min - minute
 mm – millimeter
 mL - mililiter
 N/A – Not applicable
 PLC – Programmable logic controler
 PMS – Particule Monitoring System
 SAT – Site Acceptance Test
 SCADA – Supervisory Control and Data Acquisition
 RABS – Restricted Access Barrier System
 OQ – Operational qualification
 URS – User Requirements Specification
 V – Volt

6. **ATTACHMENTS**

Attachment 01- Layout of Filling room

7. **CHANGE HISTORY LOG**

Doc. Version No.	Description of change	Change No., TrackWise record No. (if applicable)	Author of change	Date
01.00	New Document	N/A	N/A	N/A