User Requirement Specification (URS)

For Skid Filtration

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Prepared By	Technical Department Project Department Quality Assurance	F.GH	12/16/2023
Project manager	Eng. Khajeh		12/16/2023
QA Manager	Dr. Keshavarz		12/16/2023
Production Manager	Dr. Yousefy		12/16/2023
Technical Manager	Eng. Mohammadshahi	M.SHAHI 23DEC2023	12/16/2023
Responsible Pharmacist	Dr. Torabi		12/16/2023

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2. Purpose and Scope

The objective of this URS is to define and document the requirements of the User Requirement Specification for **two** movable Skid filtration systems for sterile filtration purposes at SinaDarou Pharmaceutical site. These requirements will assure that skid filtration systems will correctly and reliably perform its intended functionality.

This specification covers the design, manufacture, installation, testing and documentation of the skid filtration systems for SinaDarou pharmaceutical company.

3. Responsibility

The Supplier of the system is required to adhere to the content of this document; any deviations proposed must be clearly identified and justified by the Supplier

4. Overview

These Two skid filtration systems are based on cartridge filtration technology and must be designed to ensure the removal of micro-organisms and other contaminants by microfiltration and will be used for Clarification, filtration, microorganism's retention purposes. These systems are required for filtration of 1000 LPH and 6000 LPH in production process and they will be installed in Holding area at SinaDarou new production site.

5. Operational Requirements

5.1 Function

5.1.1 The system shall use disposable filter cartridges which are intended for filtration of *pharmaceutical products.*

5.1.1 Equipped with two filter stages, one filter stage for disc filtration and a pump

5.1.1.1 Prefiltration Step shall be done with filter cartridge 0.65 µm;

5.1.1.1 *Final Filtration step shall be done with Sartorius mini filter cartridge, 0.22 µm; Polyethersulfone(PES)*

5.1.1.2 polyvinyl difluoride (PVDF) filters *0.22 µm; for Latanoprost and Coprost eyedrops*

5.1.2 The system must be capable of connecting to the disc filter housing for utilizing polyvinyl difluoride (PVDF) filters *0.22 µm; for Latanoprost and Coprost eyedrops.This housing should be parallel with two filter stages and* Selection between filtration stages must be possible.

5.1.3 The system must be connected to the existing Clean In Place (CIP) system

5.1.4 The system shall be connected to the existing SCADA system.

5.1.5 System Applications are as following:

5.1.5.1 Clarification, filtration, microorganisms retention

5.1.6 Efficiency and safety:

5.1.6.1 Total process control with temperature and pressure sensors.

5.1.7 fully drainable skids by gas (compressed air/Nitrogen) to ensure no water comes into contact

with media fluid.

5.1.8 The system shall be capable of performing Automated sterilization cycle (121°C)

5.1.9 Filter housing specification:

5.1.9.1 Must have connection for Integrity testing filter

5.1.9.2 Housings for 2×10" cartridge filters

5.1.9.3 Housings for Disc filter for viscous liquids .

5.1.9.4 Filter housing must be made of SS 316L

5.1.9.5 Filter housing must have vent valve

5.2 connection

5.2.1 First skid filtration inlet and outlet connection: 2"

5.2.2 second skid filtration inlet and outlet connection: 1 1/2"

5.3 Process Control, Data & Security

5.3.1 Advanced control panel with touch screen interface shall be connected to the existing SCADA system

5.3.1 Sterilization report (print or electronic)

5.3.2 Filter integrity test & report

The electrical requirements shall be provided as following:

5.3.3 Equipment and component standards of the supplier may be used, with respect of local market. All components and materials have to be listed and approved by the customer.

5.3.4 All parts have to be grounded.

5.3.5 In the control-cabinet at least 30% of spare place has to be left over.

5.3.6 The control-cabinet has to be designed so that the part for the power supply and the part for the controller devices are kept separate.

5.3.7 Allowed temperature of the components within the control-cabinet from +5°C to 35°C (EN 60204) has to be ensured.

5.3.8 All wires have to be numbered on both sides, external from connector block inside the control cabinet.

5.3.9 All data lines have to be shielded.

5.3.10 Free access to the connectors and devices in the control-cabinet.

5.3.11 Separate laying of the data line and the line for the power supply.

5.3.12 Control voltage 24 V DC

5.3.13 Two supply connections have to be foreseen, one for UPS and one for direct power

connection with emergency power.

5.3.14 The control cabinets are either integrated in the equipment or above on the suspended ceiling in the technical area

5.4 The system must unify upstream and downstream machines to work simultaneously Pre-set maximum and minimum values in the parameter setting to prevent user settings over the range

5.5 Equipment failure can be analyzed by failure analysis system comes with equipment diagnostic functions

5.6 Suppliers can archive remote diagnosis through the network for the production line

5.7 Drive: Protection class must be at least IP54

5.8 PLC for process control and data acquisition. Operating panels of this equipment will be mounted in the technical area and switch panel in the hygienic class D area.

5.9 The controller has to be connected to a UPS-system. In case of power supply failure of the machine has to stop in a safe condition. The needed UPS-capacity for this step has to be specified, backup time at least 1h.

5.10 Emergency-stop buttons has to be provided in all dangerous zones

5.11 Protection class: at least IP 54 according to DIN 40065

5.12 System / equipment suitable for nominal voltage 400 V (three phases) according to DIN IEC 38. System / equipment suitable for rated frequency 50 Hz ± 10%.

5.13 All drives will be switched on directly (without delta-wyes).

5.14 The system has to be designed and built in accordance to the Low Voltage Directive (LVD) 73/23/EEC

5.15 Protection against overload is required.

5.16 Protection against short circuit is required.

5.17 Cross-sectional areas and connections of the protective conductor according to EN 61010-1. Insulating resistance according to EN 60204-1 and VDE 0100 T610.

5.18 Voltage test according to EN 60204 and VDE 0100 T610.

5.19 Residual voltage test according to EN 60204.

5.20 Every electric circuit, that has to be grounded, has to be connected to one central grounding point. The connection to the 0-potential will be provided on site.

5.21 Solvable 0-voltage connections of the control low voltage to the grounding system have to be established.

5.22 0-voltage connections of the devices with low voltage outlet have to be established.

5.23 An emergency-stop has to be at every dangerous place.

5.24 Safety devices cannot be circumvented on an easy basis or be disabled.

5.25 Safety devices operate directly in the circuit.

5.26 An emergency-stop should be within the reach for the operation personnel.

5.27 A simple calibration, recalibration, repair or exchange of the measuring device (sensor and transformer) must be possible. Necessary cable lengths for a replacement and calibration of the sensor next to the machine have to be allowed for. The line must be adjustable.

5.28 The software of the automation has to accomplish the following functional requirements:

5.28.1 Automated process execution and visualization

5.28.2 Automated registration of the measured process values, including a graphical analysis of these data

5.28.3 Monitoring of the critical process values within limits (warning and action limit)

5.28.4 Automatic alarm in case of an overstepping of a critical value and in case of failure

5.28.5 Reporting

5.28.6 Calibration

5.28.7 User administration

5.28.8 Archiving, backup of acquired data online via external system

5.29 Consecutively the requirements for the individual functional requirements are specified

5.30 The software for the process execution, data acquisition, data processing and reporting has to be projected, created, tested and documented according to GAMP Vol.5.

5.31 The software of the automation for the process execution, data acquisition, data processing and data archiving has to be compliant to 21 CFR Part 11 and has to be validated.

5.32 The software has to be organized in at least three levels:

5.32.1 Field level (Standard signals: 24 V DC for I/O-signals; 4 - 20 mA for analogue signals; Field bus Profibus DP for valves)).

5.32.2 Controller-level (continuous and sequential functions in the controller).

5.32.3 Recipe level for operation and monitoring (Recipe level in the PC-System).

5.33 The analogy signals are directly wired to the field bus.

5.34 Standard sequence structure:

The standard sequence structure (typical) must have, according to the state transition diagram, the following branches:

5.34.1 RUN

5.34.2 ABORT

5.34.3 HOLD

5.34.4 S-HOLD

HOLD means that the sequence remains in the actual step and the transition to the next step is blocked.

S-HOLD means that in case of equipment failure a safe mode of operation has to be ensured at all times by proper means. The machine has to stay in safe operation mode without taking any damage or inflict damage on other systems in case of equipment failure.

If the HOLD status is not directly managed by the supervision, other solutions included in the freeze-drying cycle can be accepted. This point will be studied during DQ.

Data integrity:

New or changed raw data sets are not allowed to overwrite existing data.

5.35 In case of instrument air failure, safe mode of operation has to be assured at all times. In case of electrical power failure, safe mode of operation has to be assured at all times.

5.36 In case of electrical power failure, safe mode of operation has to be assured at all times

5.37 In case of electrical power failure, the requested UPS must buffer and safe all relevant process data and must assure secure and reliable system shut down after a certain period of power failure.

5.38 In case of no sufficient utilities the operation has to stop in a second way.

5.39 Ventilator (control cabinet) failure must be indicated by an alarm. Not included in control system.

5.40 In case of ventilator (control cabinet) failure process start is interlocked.

5.41 Active processes must not be aborted.

5.42 High temperature in the control cabinet must be indicated by an alarm message. A thermostat in the control cabinet and the contact will be added to the GTC (GTC) signal.

5.43 In case of high temperature in the control cabinet process start is interlocked. No report of the signal to POLARIS 2 supervision (only hardware contact).

5.44 Active processes must not be aborted.

5.45 Motor protection failure must be indicated.

5.46 Line safety switch failure must be indicated.

5.47 Remote assistance, maintenance must be documented in a readable log-file.

5.48 System and application access are only allowed with user-ID and password.

5.49 The password must be changed periodically.

5.50 An alarm has to provoke the following:

5.50.1 Coloured identification at the visualization.

5.51 Acoustic signal

Alarm messages, warning messages and user notifications have to differ from each other and have different priorities which need to be visualized accordingly.

5.51.1 Priority 1: System messages (system failure).

5.51.2 Priority 2: Malfunction message (motor protection switch, sensor breakage etc.)

5.51.3 Priority 3: Alarm messages (action limit)

5.51.4 Priority 4: Warning messages (warning limit)

5.51.5 Priority 5: Operation notification (information for the operator)

5.52 2 alarms levels can be proposed with the use of GTC contact relayed on the supervision, with for example a flash lamp. Details to be approved during the DQ.

5.53 System, malfunction, alarm and warning messages must be classified in different categories. According to the category the system reacts different:

5.53.1 Category 1: System returns in initial safe state.

5.53.2 Category 2: Active processes are aborted.

5.53.3 Category 3: Non-influence on the active process.

5.54 According to the alarm, the system will react according to the 3 mentioned categories but alarms are not classified in categories.

5.55 All alarm notifications have to be documented with the following information:

5.55.1 Date and time of the alarm.

5.55.2 Description of alarm.

5.55.3 Date and time of alarm acknowledgement.

5.55.4 Date and time of alarm end / confirmation.

5.55.5 Who has confirmed the alarm?

5.55.6 Critical alarm stops the machine

5.56 Alerting and failure:

As a minimum following alarm messages must be configured and displayed:

5.56.1 Power failure

5.56.2 Emergency button actuated

5.56.3 Motor safe guard

5.56.4 Run time error valve

5.56.5 PLC failure

5.56.6 Program aborted

5.56.7 Program run time error

6. Environment

6.1 Indoor location with dry surfaces and walls
6.2 No direct or indirect exposure to sunlight
6.3 Min. / max. operating temperature between 18°C and 28 °C
6.4 Maximum humidity: 50%
6.5 Utilities:
- 6.5.1 compressed air 1 bar
- 6.5.2 nitrogen gas 1 bar
- 6.5.3 nitrogen gas 2.5 bar

7. Constraints

7.1 Equipment Constraints

The space dedicated to fit the appliance in the Holding room is limited. The approximate space available is 0.5 meter (W) × 1 meter (L) × 1.6 meter(H)

7.2 Compatibility and Support

The equipment shall be completed in all respects, comply with GAMP 5 and cGMP standards for cleaning and ne verified as being in the correct order to enable full process validation to be performed., efficient, safe and secure operation and maintenance and shall have its systems tested

7.3 Availability/Maintenance

The System shall be maintained on a schedule as indicated by the supplier. Supplier is to provide (at minimum) the following maintenance instructions:

7.3.1 A comprehensive recommended maintenance (regular recommended inspection intervals, wear points, recommended spare parts list)

7.3.2 Supplier shall supply Operation, Installation, Maintenance manuals

7.4 Milestones and Timelines

The skid filtration systems shall be installed, commissioned and ready for operation till **June 2024**

7.5 Access Level

Different access levels for users:

7.5.1 operator,
7.5.2 supervisor,
7.5.3 administrator,
7.5.4 maintenance

8. Lifecycle

8.1 Testing

8.1.1 Functional Design Specification (FDS)

8.1.2 Factory Acceptance Test (FAT)
8.1.3 Commissioning

8.1.4 SAT protocol

8.1.4 Installation Qualification (IQ)
8.1.5 Operational Qualification (OQ)
8.1.6 Gassing Cycle Development (GCD)
8.1.7 Performance Qualification (PQ)

Factory Acceptance Test (FAT) may include but not limited to the following Inspections:

8.1.8 Dimension and layouts
8.1.9 Connection size, orientation, position as drawings
8.1.10 Components and instrumentation as required
8.1.11 Materials and surface finish to the specification
8.1.12 documentation (certificates and drawing)

8.2 Delivery/ Documentation

Supplier should supply the documentation, and the machine test qualifications, including:

8.2.1 Installation drawing,
8.2.2 P&ID,
8.2.3 Electrical wiring diagram,

8.2.4 As Built drawing,
8.2.5 Operating Manual
8.2.6 Maintenance Instructions
8.2.7 Safety Instructions
8.2.8 Comprehensive recommended spares parts list.
8.2.9 FAT Protocol
8.2.10 SAT Protocol
8.2.11 Design qualification
8.2.12 Installation qualification documents
8.2.13 Operational qualification documents
8.2.14 Calibration certificates
8.2.15 Alarm list
8.2.16 Component list
8.2.17 Parts List / Mechanical and Electrical

8.3 Support and training

Training course should be performed by manufacturer on site

9. References

9.2.2 USP 43
9.2.3 CFR11, 21, 210, 211, 600 & 610
9.2.4 PICS

10.Definitions, Acronyms and Abbreviations

DQ = Design Qualification
FAT = Factory Acceptance Test
USP = United States Pharmacopoeia
HMI = Human-Machine Interface
P&ID = Piping and Instrumentation Diagram
cGMP = Current Good Manufacturing Practice
IQ = Installation Qualification
OQ = Operational Qualification
SAT = Site Acceptance Test
PICS = Pharmaceutical Inspection Co-operation Scheme

11.Document Distribution

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Original version	Project Department
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