**UserRequirementSpecification(URS)**

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Purpose

These usersRequirementSpecification(URS) describes the user's requirementstoaffectedPremisesfor[ Place of deployment For example: Buildings]and includes the functional, operational and data requirements forthe systems.

MissionArea

With this URS, the requirements fortheaffected==References==RR Monitoring)for[ Place of deployment For example: Buildings]in the case of:[ Name of customer, address]==References==

Terms and abbreviations

Definitions

**Water qualities**

|  |  |
| --- | --- |
| Name / Abbreviation | Use |
| GxP | Abbreviated when several of the practice rules in the fields of "GCP" (Good Clinical Practice), "GDP" (Good Distribution Practice), "GFP" (Good Practice) or "GMP" (Good Manufacturing Practice) are affected. |
| HEPA filters | High efficiency particulate filters Air filter) |
| Information (data) | e.g. numbers, texts, images, videos or audio files |
| Product quality | GMP-critical product specifications (e.g. according to Design History File) |

Abbreviations

|  |  |
| --- | --- |
| Definition / Abbreviation | Explanation |
| DQ | Design qualification |
| FMEA | Failure Mode Effects Analysis (Failure Mode Effects Analysis) |
| GMP | Good Manufacturing Practice |
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|  |  |

UserRequirements(User requirements)

Dhe qualification is based on a risk-based approach. The qualification process and the regulatory classification are described in the system-specific qualification master plan (QMP).Based on GMP relevance analyses, the system «clean space» (Doc ID GMP-I\_GRA\_RR) and the system «clean space monitoring» (Doc ID GMP-I\_GRA\_RR\_MS) were classified as GMP relevant.

TheURSwillclassified according to their relevance (GxP or security/economicity) and criticality (necessary/optional).

GxP- No, no, no, no, no, no, no.relevant points must be taken into account in the qualification; Securitys-/Economy- No, no, no, no, no, no, no.relevant points must be taken into account by the engineering/operator.Requirements, which are classified as "necessary", must be implemented, for "optionally classified points can possibly be applied to the implementationthe requirement is waived.

In the column "URS#" of these URS, direct requirements are marked with a number. This number shall consist of the chapter number of the URS and a serial number..

4.1Technical standards

The interpretation and execution to the affectedMedia(Production, storage and distribution) must comply with relevant local, regional and national regulations (European Union, USA)and correspond to the level ofTechnology.

Requirements

4.2.1General requirements[Cleanrooms]

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| URS# | Description | Classification |
| GMP spacebook | GMP spacebook | GMP spacebook |
| 4.2.1 | Number and size, including marking of the rooms, as well as specification of the zone status for pure rooms and material, including lock systems | GxP, necessary |
| Zone status and transitions | Zone status and transitions | Zone status and transitions |
| 4.2.1-3 | Zone status of cleanrooms according to GMP space book (Annex 1): CNC RRK D RRK C Transition CNC to RRK D Transition RRK D to RRK C | GxP, necessary |
| 4.2.1-4 | Zone status Material passing between E20 and E21: RRK C | GxP, necessary |
| 4.2.1-5 | Access from a cleanroom class (RRK) to the next higher RRK is via locks The lock corresponds to the higher RRK (Annex 1) | GxP, necessary |
| 4.2.1-6 | Spatial separation within the lock is carried out by barriers (Sit-Over-Bank or soil marking) | GxP, necessary |
| Rivers (material flow, personnel flow) | Rivers (material flow, personnel flow) | Rivers (material flow, personnel flow) |
| 4.2.1-7 | Separation of material and personnel flow: By means of material and personnel locks, as well as material | GxP, necessary |
| 4.2.1-7 | Spatial separation of material and personnel flow: Materials are applied via material lock Within production rooms, materials can be passed through material People are entered or left the cleanroom via personnel locks. | GxP, necessary |
| 4.2.1-8 | Biological waste (solid material) is applied via autoclaves | GxP, necessary |
| Cleanroom conditions | Cleanroom conditions | Cleanroom conditions |
| 4.2.1-9 | Cleanroom conditions of the individual rooms incl. Warning limits according to GMP space book (Annex 1): pressure pressure difference temperature Moisture Discontinuous monitoring for particles and microbiology | GxP, necessary |
| 4.2.1-10 | Pressure difference between space zones is measured against "empty tube" instead of "side room" | GxP, necessary |
| Flow | Flow | Flow |
| 4.2.1-11 | Flow direction in the room takes place from critical to less critical area | GxP, necessary |
| 4.2.1-12 | Non-laminar low-turbulence current must be guaranteed | GxP, necessary |
| 4.2.1-13 | Cleanroom conditions in the locks correspond to the higher RRK (Annex 1) | GxP, necessary |
| 4.2.1-14 | The cleanroom conditions must be monitored and observed (monitoring) | GxP, necessary |
| Maintenance/maintenance | Maintenance/maintenance | Maintenance/maintenance |
| 4.2.1-15 | Systems must be maintainable | GxP, necessary |
| 4.2.1-16 | Revision flaps are available for maintenance between RR suspended ceiling and building rough ceiling (plenum) | GxP, necessary |
| 4.2.1-17 | Exchangeable wall modules: The wall and ceiling modules should be installed in such a way that they are individually accessible and easily interchangeable. | GxP, necessary |
| Calibration | Calibration | Calibration |
| 4.2.1-18 | Sensors must be: calibrated (plant calibration) recalibratable (calibration preferably in built-in condition or simple disassembly) | GxP, necessary |
| Control panel | Control panel | Control panel |
| 4.2.1-19 | Control panel for monitoring the cleanroom parameters | GxP, necessary |

Environmental conditions/interfaces

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| --- | --- | --- |
| URS# | Description | Classification |
| 4.2.2-1 | Location Building GMP-I is [Location] | GxP, necessary |
| 4.2.2-2 | Interface cleanroom/ Ventilation system: final HEPA filter (Specification H14) incl. scan certificate | GxP, necessary |
| 4.2.2-3 | Flush separators in the exhaust air shall be provided in personnel locks | GxP, necessary |
| 4.2.2-4 | The material is actively ventilated (cleanroom class C) | GxP, necessary |
| 4.2.2-5 | Interface cleanroom/ventilation system: suction arm in the process room 4, connected to central extraction system | GxP, necessary |
| 4.2.2-6 | Interface cleanroom/ventilation system: LF-zone-digestorium with own supply and exhaust air | GxP, necessary |

Media coverage

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| URS# | Description | Classification |
| 4.2.2.1 -1 | The following media connections in cleanrooms (Annex 2): Compressed air Oxygen Purified Water (PW) | GxP, necessary |
| 4.2.2.1-2 | Media (for techn. Supply/operation of plants/systems) such as cooling water and compressed air are available | Safety, necessary |

Construction requirements

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| --- | --- | --- |
| URS# | Description | Classification |
| 4.2.3-1 | Building shell is not external shell (double shells when RR closes outwards, room in room system) | GxP, necessary |
| 4.2.3-2 | Premises and impact/disposal points to withstand the planned overpressure cascade | GxP, necessary |
| 4.2.3-3 | The rooms are to be executed in white (RAL 9010) | GxP, necessary |
| 4.2.3-4 | For RR walls with window elements double glazed (frameless) VSG discs flush to integrate into the frame | GxP, necessary |
| 4.2.3-5 | Doors with windows in the upper area are used | GxP, necessary |
| 4.2.3-6 | Doors are opened electronically. There is a holding mechanism for double doors. | GxP, necessary |
| 4.2.3-7 | Emergency lamps shall be installed in the grid lamps or on the cleanroom ceiling | GxP, necessary |
| 4.2.3-8 | For windows in the open, appropriate darkening possibilities shall be provided on the outside. They're supposed to be wind stable. | Safety, necessary |
| 4.2.3-9 | Ceiling lamps shall be flush-in and sealed/sealed with suitable plastic (e.g. silicone) | GxP, necessary |
| 4.2.3-10 | Ventilation: tightness class sewer network Class C according to DIN EN 1507 for square air ducts and DIN EN 12237 for round air ducts | GxP, necessary |
| 4.2.3-11 | Flow-technical favourable channel guidance (to avoid too many angles) | GxP, necessary |
| 4.2.3-12 | All lines (electrical, media) are to be laid into the wall elements (well space of the walls) Alternatively, selective media columns are allowed | GxP, necessary |
| 4.2.3-13 | Media execution (mousehole) is available at the intended position: Transition Process Space 4 GMP1\_E.16 to Process Room 2 GMP1\_E.20 in number 3 pieces - Diameter 4-6 inches - Installation height 950 mm FBK Process Room 1 GMP1\_E.15 to Process Room 2 GMP1\_E.20 in number 1 piece - Diameter 4-6 inches - Installation height 950 mm FBK | GxP, necessary |
| 4.2.3-14 | Media entry systems Wall ceiling (cable/pipe) shall be closed airtight and flush-mounted. | GxP, necessary |
| 4.2.3-15 | A shock protection is in relevant places. (e.g. material lock) | Safety, necessary |
| 4.2.3-16 | Detachment arm in the process room GMP1\_E.16 mounted on the cleanroom wall and connected to exhaust air system of the central RLT system | GxP, necessary |
| 4.2.3-17 | LF zone/digestorium in the process room GMP1\_E.15 with connection to the RLT for supply air as 75 % fresh air and 100 % exhaust air via HEPA 14: Internal surface Size (useful surface) is 2.3 m long, 0.7 m deep, 1 m height 6 sockets in the inner surface, lateral introduction / connectors for hoses walls: glass/transparent LF housing made of material stainless steel LF zone is open in operation (without discs) with air barrier through the air flow interface: Communication with RLT system over potential free contact (When the system is switched on, the RLT system receives a signal that more air is to be provided in the room and vice versa) | GxP, necessary |
| 4.2.3-18 | The cleanroom wall and wall elements axis A-1; A-2, on the entry opening, must be removable for application area 2000 mm x 2250 mm and re-sealable after entry (magnetic coupling) and sealed. | GxP, necessary |

Drawings and plans

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| URS# | Description | Classification |
| 4.2.3.1-1 | Creation and delivery of production drawings, R&I flow diagrams, schematics, ceiling grid drawings incl. lighting, topology of the cleanroom Monitoring system (PDF and DWG format) for RR and RLT Uniform component marking in R&I and drawings. | GxP, necessary |

Material/surfaces

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| URS# | Description | Classification |
| 4.2.3.2-1 | Hygienic Design: Smooth, free of cracks, dense, easy to clean/ disinfectable surfaces cracks, sharp edges and dead spaces are to be avoided hollows to wall and machine connections are to be manufactured and flush well cleanable | GxP, necessary |
| 4.2.3.2-2 | Floor covering: anti-slip dissipative low particle abrasion | GxP, necessary |
| 4.2.3.2-3 | Interior Material rich easy to clean | GxP, necessary |
| 4.2.3.2-4 | Surfaces are resistant to the cleaning and disinfection agents used by [company] (alcoholic solvents) | GxP, necessary |
| 4.2.3.2-5 | Seals: must be resistant to abrasion and ageing and as far as possible UV-resistant must not release particles and plasticizers | GxP, necessary |
| 4.2.3.2-6 | Fittings/machine connections, LF zone and extraction arm in the RR must be made of stainless steel (min. 1.4301) | GxP, necessary |
| 4.2.3.2-7 | Lubricant: must be min. Have food quality (proof of compliance according to NSF-H1) TSE certified (free of materials of animal origin) | GxP, necessary |
| Furnishing furniture | Furnishing furniture | Furnishing furniture |
| 4.2.3.2-8 | Furniture must be flush to the ceiling or 25°-30° bevelled. Furniture should correspond to "hygienic design". | GxP, necessary |
| 4.2.3.2-9 | Furniture should be made of stainless steel | GxP, necessary |

Performance data

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| URS# | Description | Classification |
| 4.2.3.3-1 | Ventilation (Annex 1): Supply air Exhaust air Air quantities | GxP, necessary |
| 4.2.3.3-2 | Air change corresponds to RRK | GxP, necessary |
| 4.2.3.3-3 | Ratio of fresh air 100 % in all cleanrooms | GxP, necessary |

Safety requirements

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| URS# | Description | Classification |
| 4.2.4.1 | A mutual lock locking is necessary for the locks | GxP, necessary |
| 4.2.4.2 | A mutual lock lock is necessary for the material to pass through | GxP, necessary |
| 4.2.4-3 | Lock doors and quick-run doors shall be fitted with an emergency switch | GxP, necessary |
| 4.2.4-4 | Storage space GMP1\_E.12 should be subject to access control | GxP, necessary |
| 4.2.4-5 | Precautions must be taken against the intrusion of insects and other animals (Pest Control) | GxP, necessary |
| 4.2.4-6 | All electrical and EMSR-side components shall comply with the respective environmental requirements in order to ensure safe operation of the system. | Safety, necessary |

Process requirements

Material flow IN

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| URS# | Description | Classification |
| 4.2.5.1-1 | Materials: Storage of materials in the central outer warehouse Transport to the GMP-I building Delivery via GMP1\_E.07 Installation via material locks in respective production rooms Transfer between production rooms by means of material | GxP, necessary |
| 4.2.5.1-2 | Repackaging Materials: in GMP-I building no wood (pallets either stainless steel or plastic) no cardboard in GMP-I | GxP, necessary |

Material flow OUT

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| URS# | Description | Classification |
| 4.2.5.2-1 | Storage material/product in storage room GMP1\_E.12 | GxP, necessary |
| 4.2.5.2-2 | Materials: Application via material lock Transport in storage Storage Equipment in storage Transport and handover e.g. to customer via GMP1\_E.07 (after QC release) | GxP, necessary |
| 4.2.5.2-3 | Separate flows of materials and product | GxP, necessary |

Persons

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| URS# | Description | Classification |
| 4.2.5.3-1 | Number Persons in locks in accordance with the GMP Room Book (Annex1) | GxP, necessary |
| 4.2.5.3-2 | A clothing concept is defined (Annex 3) | GxP, necessary |

Functional requirements

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| URS# | Description | Classification |
| 4.2.6-1 | Lock lock: Automatic locking and display system | GxP, necessary |
| 4.2.6-2 | Release Lock locking after parameterised time or after reaching specified RR conditions) | GxP, necessary |
| 4.2.6-3 | Opening Lock doors in case of fire alarm | Safety, necessary |
| 4.2.6-4 | Lock doors and quick-run gates trigger an alarm when opened too long | GxP, necessary |
| 4.2.6-5 | Monitoring of spatial conditions: Starting alarms Normal condition: no alarm freezing/delay time: no alarm over/underrun: alarm (acoustic or visual) | GxP, necessary |

Monitoring

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| URS# | Description | Classification |
| 4.2.7-1 | Display cleanroom conditions on PAL GMP1\_E.11 (e.g. pressure difference) | GxP, necessary |
| 4.2.7-2 | Delay time/freezing available for alarming (by short opening of lock doors | GxP, necessary |
| 4.2.7-3 | Determined pressure difference monitoring between different cleanroom classes must be available and continuously monitor | GxP, necessary |
| 4.2.7-4 | The system must be able to trigger alarms in case of breach of warning limits and alarm limits | GxP, necessary |
| 4.2.7-5 | Pressure differential monitoring shall: Deactivate alarm | GxP, necessary |
| 4.2.7-6 | Monitoring documents including monitoring data must be easily accessible to users (identification via signal lamp and receipt via control computer) | GxP, necessary |
| 4.2.7-7 | Data (monitoring) is recorded and archived | GxP, necessary |
| 4.2.7-8 | Data must be protected against tampering by unauthorised persons and loss (within the organisation as well as during transmission) | GxP, necessary |
| 4.2.7-9 | Data must be readable for the entire retention period (up to 30 years) | GxP, necessary |
| 4.2.7-10 | Temperature control for the average formation of individual rooms, unless otherwise specified | GxP, necessary |
| 4.2.7-11 | Trends: daily and monthly accurate display and evaluation possible | GxP, necessary |
| 4.2.7-12 | An overview of maintenance and malfunction messages in the system shall be presented; This includes, in particular, warning and alarm messages | GxP, necessary |

Requirements for security and access and authorisation controls

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| URS# | Description | Classification |
| 4.2.7.1-1 | The software program system must be protected by physical access control and changing password rules | GxP, necessary |
| 4.2.7.1-2 | The system must provide for several levels of security depending on the responsibilities of the user (only RRM) | GxP, necessary |
| 4.2.7.1-3 | Audit Trail: Generation and reliability. | GxP, necessary |
| 4.2.7.1-4 | Non-response operation incl. Data storage by UPS (interruptible power supply) | GxP, necessary |

Backup and recovery requirements

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| URS# | Description | Classification |
| 4.2.7.2-1 | The system must have backup and recovery functionality. An emergency programme for this purpose must be documented | GxP, necessary |

Data Integrity Requirements

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| URS# | Description | Classification |
| 4.2.7.3-1 | The system generates electronic records as defined in 21 CFR 11, EU-GMP Annex 11 and other pharmaceutical IT regulations | GxP, necessary |
| 4.2.7.3-2 | Electronic data is archived via interface in the in-house server | GxP, necessary |

Hardware requirements

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| URS# | Description | Classification |
| 4.2.7.4-1 | Standard hardware components of well-known manufacturers shall be used | GxP, necessary |

Software requirements

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| --- | --- | --- |
| URS# | Description | Classification |
| 4.2.7.5-1 | Standard software components of well-known manufacturers are to be used (e.g. Microsoft Windows, Microsoft SQL database) according to GAMP requirements | GxP, necessary |
| 4.2.7.5-2 | Safety patches and updates are provided by the maintenance technician during the inspection/ Maintenance installed | GxP, necessary |

Documentation and training requirements

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| URS# | Description | Classification |
| 4.2.8-1 | The complete documentation must be in German | GxP, necessary |
| 4.2.8-2 | The documentation shall: 1-fold in paper form (stitched in DIN A4 folders including table of contents) and delivered on a data carrier (USB stick) | GxP, necessary |
| 4.2.8-3 | An overview list of all delivered supplier documents shall be submitted to the client. | GxP, necessary |
| 4.2.8-4 | Uniform marking of all components and components in all documents | GxP, necessary |
| 4.2.8-5 | All fittings/ The sampling points shall be clearly marked in accordance with the flow diagrams. | GxP, necessary |
| 4.2.8-6 | The version control of all manufacturer documents must be ensured by means of a change history | GxP, necessary |
| 4.2.8-7 | All documents must be available until acceptance (SAT) final | GxP, necessary |
| 4.2.8-8 | EC declaration of conformity for all components of the scope of delivery | GxP, necessary |
| 4.2.8-9 | CE marking | GxP, necessary |
| 4.2.8-10 | Initial calibration of the sensors | GxP, necessary |
| 4.2.8-11 | Function description | GxP, necessary |
| 4.2.8-12 | Hygiene inspection according to VDI 6022 for ventilation | GxP, necessary |
| 4.2.8-13 | Recommendations/Guides incl. Manufacturer's maintenance/maintenance schedules Excluded are revision openings (maintenance-free) | GxP, necessary |

Lists

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| --- | --- | --- |
| URS# | Description | Classification |
| 4.2.8.1-1 | List of spare parts with recommendation on storage | GxP, necessary |
| 4.2.8.1-2 | Wearing sub-list | GxP, necessary |
| 4.2.8.1-3 | Warning and alarm list (listing and explanation of all alarm functions and error messages depending on the operating state including system response (light, horn, shutdown)) | GxP, necessary |
| 4.2.8.1-4 | Parameters list A separate list of parameters is not necessary for the components of the RLT system (H14 filters, drain outlets and ground extraction). | GxP, necessary |
| 4.2.8.1-5 | Component List | GxP, necessary |
| 4.2.8.1-6 | Filter lists | GxP, necessary |
| 4.2.8.1-7 | List of measuring instruments | GxP, necessary |
| 4.2.8.1-8 | A measuring station plan shall be drawn up. | GxP, necessary |
| 4.2.8.1-9 | A calibration list for relevant measuring points with description and acceptance criteria shall be drawn up. | GxP, necessary |
| 4.2.8.1-10 | A maintenance specification list shall be created. | GxP, necessary |

Electrical documentation

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| URS# | Description | Classification |
| 4.2.8.2-1 | A cable list/ Create MSR list | GxP, necessary |
| 4.2.8.2-2 | A schematic must be available in "as-built" version | GxP, necessary |

Operator documentation

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| URS# | Description | Classification |
| 4.2.8.3-1 | Logbooks must be present or created if not initially present | GxP, necessary |
| 4.2.8.3-2 | Technical data sheets or manuals shall be provided | GxP, necessary |
| 4.2.8.3-3 | Instructions for operation/security/maintenance: building hygiene (e.g. cleaning instructions, functioning pest control system) of the rooms (maintenance, maintenance, calibration, operation) and cleanroom conditions (monitoring) | GxP, necessary |

Material quality

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| --- | --- | --- |
| URS# | Description | Classification |
| 4.2.8.4-1 | At least tooling 2.2 is required for materials that are product-related | GxP, necessary |
| 4.2.8.4-2 | Declarations of conformity according to 21 CFR 177 for product-related surfaces | GxP, necessary |
| 4.2.8.4-3 | Material certificates Seals Does not apply to RRM, as no product-contacted seals or product-contact sensors are installed and no material certificates are required. | GxP, necessary |
| 4.2.8.4-4 | Filter certificates (H14) | GxP, necessary |
| 4.2.8.4-5 | Sealing test/filter leak test | GxP, necessary |

Training requirement

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| URS# | Description | Classification |
| 4.2.8.5-1 | Initial operator training must be carried out | GxP, necessary |

Documents quoted or accompanying

GMP-I\_GRA\_RRGMP relevance analysis Systems Cleanroom

GMP-I\_GRA\_RR\_MSGMP-RelevanceAnalysisSystemsCleanroomMonitoring

EU GMP Part IIBasic requirements for active substances used as starting materials

andAnnices

VDI 6022Indoor air technology, indoor air quality

21 CFRTitle 21ofCodeofFederalRegulation

COMMUNICATIONpharmacovigilance and active substance manufacturing regulation

Annexes

GMP-I\_RR\_URS A1GMP-Spacebook

GMP-I\_RR\_URS A2Media connections in RR

GMP-I\_RR\_URS A3Clothing concept