**User Requirement Specification (URS)**

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Table of Contents

Change index

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Purpose

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

MissionArea

With this URS, the requirements fortheaffectedMedia[e.g.(pressure air, oxygen andPurifiedWater)]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 |
| City Water / SW | Production EW, use for emergency shower |
| Hardened water / EW | Production PW, use for dishwasher |
| Purified Water / PW | Buffer and media production, rinsing of glassware, cooling of the exhaust air in the fermenter, steam generation in the autoclave |
| Water for Injection / WFI | Final formulation of the final product |

Abbreviations

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| --- | --- |
| 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 a GMP relevance analysis (Doc IDGMP-I\_GRA\_GEB\_O2;Oxygen,GMP-I\_GRA\_GEB\_PW;PurifiedWaterandGMP-I\_GRA\_GEB\_DL;Compressed air),ntheMediasystemecategorised 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

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| URS# | Description | Classification |
| 4.2.1-1 | The supplied and installed components shall be clearly and permanently marked to clearly identify the medium, flow direction and gradient. | GxP, necessary |
| Maintenance/maintenance | Maintenance/maintenance | Maintenance/maintenance |
| 4.2.1-2 | The systems must be able to be maintained. In particular, the accessibility of parts of the system to be maintained must be given (if possible from outside the RR) | GxP, necessary |
| 4.2.1-3 | PW: Regular disinfection / Sanitization of the system (UV) (e.g. monthly sanitization by 80°C) Treatment for at least 30 minutes) Before release: Chemical test Microbiological results within specification | GxP, necessary |
| Calibration | Calibration | Calibration |
| 4.2.1-4 | Only calibrated sensors are to be supplied that allow easy recalibration. | GxP, necessary |

Environmental conditions/Interfaces

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| URS# | Description | Classification |
| 4.2.2-1 | Location Building GMP-I is the factory site of company, location, street | GxP, necessary |
| 4.2.2-2 | Specification regarding quality (Ph. Eur ): Microbiological Particles Chemical | GxP, necessary |
| 4.2.2-3 | Use of filters for compressed air before and after drying | GxP, necessary |
| 4.2.2-4 | Manual sampling points must be present in the system after filtering in the compressed air | GxP, necessary |
| 4.2.2-5 | Production of PW quality is done via equipment | GxP, necessary |
| 4.2.2-6 | Relevant interfaces are in Annex A1: GMP-I\_Media\_URS A1 Media Connections Described | GxP, necessary |

Media coverage

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| URS# | Description | Classification |
| 4.2.2.1 | All necessary connections for the media supply shall be provided | GxP, necessary |
| Water | Water | Water |
| 4.2.2.1-3 | Initial quality Water qualities as defined (Chapter 3.1) WFI is provided as an option for a qualitative upgrade of the PW plant. | GxP, necessary |
| 4.2.2.1-4 | Connection for heat exchanger (heating PW for sanitization) Electric cooling circuit, supply temperature 6 °C, return 12 °C Connection to process air (armatures) Process air oil-free: pressure 6.0 bar Connection to power supply Normal power supply: 3 x 230 V/400 V, 50 Hz Waste water Connection Processes of the PW-producer and the pump | Operation, necessary |

4.2.3Construction requirements

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| URS# | Description | Classification |
| 4.2.3-1 | Deteriorated execution: In principle, death dreams must be avoided | GxP, necessary |
| 4.2.3-2 | Unless otherwise specified, pipelines shall be designed in accordance with the 3-D rule | GxP, necessary |
| 4.2.3-3 | Rest emptyability possible (for pipelines a gradient of at least 1%, ideally 2%, to the consumer must be maintained) no gradient of DL and O2 | GxP, necessary |
| 4.2.3-4 | All cables are to be laid into the cleanroom wall elements (well space of the walls). Alternatively, point-by-point media columns are permitted. In the technical room, the cables can be laid as open installation, | GxP, necessary |
| 4.2.3-5 | Manually detachable connections (e.g. triclamp connections) on pressured lines shall be executed as a safety triclamp | GxP, necessary |
| 4.2.3-6 | The generator system/plants must be executed as pre-assembled compact system including pre-loading tank, ready to connect and pre-qualified with its own control in a frame frame as package unit | GxP, necessary |
| 4.2.3-7 | All pipes (PW/O2/DL) made of stainless steel (material 1.4404 (316L) or 1.4435 according to DIN 11866 Series B DF Class 2.) | GxP, necessary |
| 4.2.3-8 | Sampling points: all sampling points must be freely accessible | GxP, necessary |
| Welding | Welding | Welding |
| 4.2.3-9 | The manufacturer's pipe label shall be retained (even for shorter tubes after welding) | GxP, necessary |
| 4.2.3-10 | Welding seams shall be freed from start-up colours/pitch layers outside by pickling. Welding seams shall, as far as possible, be subjected to a penetration test. This shall be recorded. Not applicable to oxygen distribution | GxP, necessary |
| 4.2.3-11 | Inaccessible points for penetration testing are to be tested in 100% endoscopically Purge testing of welds are not required in mechanical welding. | GxP, necessary |
| 4.2.3-12 | Preferably orbital welding | GxP, necessary |
| 4.2.3-13 | Distribution: for each medium according to annex media connections (PW: ring line, avoid tap line at tap points, O2: tap line, DL: tap line) | GxP, necessary |
| Valves and detachable connections | Valves and detachable connections | Valves and detachable connections |
| 4.2.3-14 | Disaster valves: diaphragm valves (2/2-way) or ball valves Disaster valves: T- diaphragm valves | GxP, necessary |
| 4.2.3-15 | Detachable compounds: If terminal connections are required, terminal connections according to DIN 32676 shall be used | GxP, necessary |

4.2.3.1Drawings and plans

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| URS# | Description | Classification |
| 4.2.3.1-1 | Creation and delivery of R&I flow pictures (PDF and DWG format) Uniform component marking in R&I | GxP, necessary |
| 4.2.3.1-2 | Isometry of pipes (as built) with position of numbered welds In the compressed air system, pipes are pressed. | GxP, necessary |
| 4.2.3.1-3 | R&I shall be marked with medium, flow direction, gradient (no gradient in DL and O2), diameter, tank and tank details, as well as valves, filters, sampling points, waste water pipes | GxP, necessary |

4.2.3.2Material/Surfaces

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| URS# | Description | Classification |
| 4.2.3.2-1 | Hygienic Design: Smooth, free from cracks, dense cracks, sharp edges and dead dreams are to be avoided well cleanable | GxP, necessary |
| 4.2.3.2-2 | Product-contacted areas: metal. Material 1.4404 (316L) or 1.4435 according to DIN 11866 series B DF Class 2. 1.4571 may also be used for sensors. | GxP, necessary |
| 4.2.3.2-3 | Non-metallic contact parts (e.g. membranes) made of GMP-compliant plastic-free plastic. The non-metallic material of the PW conduction system shall withstand a temperature of at least 80°C. | GxP, necessary |
| 4.2.3.2-4 | Non-product-related areas: material 1.4301 or better. | GxP, necessary |
| 4.2.3.2-5 | Surface finish product touching: Ra≤0.8 μm, electropolished | GxP, necessary |
| 4.2.3.2-6 | Internal surfaces of the pipelines should be oil-/fat-free. Pipes should be tested for tightness (test pressure ≥1.5 x operating pressure). | GxP, necessary |
| 4.2.3.2-7 | Filter: maximum pore size 0.22 μm | GxP, necessary |
| 4.2.3.2-8 | Lubricant: must be min. Food quality (proof of compliance with NSF-H1) TSE certified (free of materials of animal origin) | GxP, necessary |
| 4.2.3.2-9 | Initial cleaning and passivation of water pipes | GxP, necessary |

4.2.3.3Performance data

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| URS# | Description | Classification |
| Purified Water | Purified Water | Purified Water |
| 4.2.3.3 | The system shall meet the specifications for PW generation and distribution. | GxP, necessary |
| Compressed air | Compressed air | Compressed air |
| 4.2.3.3-9 | Compressed air (ISO 8573-1 class 1.2.1 to be monitored): Operating pressure: ≥6.0 bar (ü) | GxP, necessary |
| Oxygen | Oxygen | Oxygen |
| 4.2.3.3-10 | Oxygen (to be monitored): Operating pressure: ≥9,0 bar (ü) | GxP, necessary |
| 4.2.3.3-11 | Name/declaration Product: ‘Oxygen KW-free' Specification: Purity: ≥ 99,6 % H20: ≤ 5 ppm KW: ≤ 0,1 ppm CO2: ≤ 1 ppm N2 + Ar: ≤ 4000 ppm (Figures are to be understood as ideal volume components (= molan parts)) | GxP, necessary |

Safety requirements

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| URS# | Description | Classification |
| 4.2.4.1 | Pipe systems shall be safe to relax. | GxP, necessary |
| 4.2.4.2 | After switching off the main energies as well as in the event of a failure of the main energy, the affected system or sub-installation must go into a safe state. When the energy returns, the system must not restart automatically. No risks to affected systems/systems may be present. Sub-assets | Safety, necessary |
| 4.2.4-3 | Installations shall be designed in accordance with Machinery Directive 2006/42/EC. | Safety, necessary |
| 4.2.4-4 | Containers and lines covered by the Pressure Equipment Directive shall be designed in accordance with 2014/68/EU. | Safety, necessary |
| 4.2.4-5 | All electrical equipment shall be designed in accordance with Low Voltage Directive 2006/95/EC. | Safety, necessary |
| 4.2.4-6 | Noise pollution: The generator system has a maximum sound pressure of 80 dB(A). | Safety, necessary |
| 4.2.4-7 | All electrical and EMSR-side components shall comply with the respective environmental requirements in order to ensure safe operation of the system. | Safety, necessary |
| Oxygen | Oxygen | Oxygen |
| 4.2.4-8 | Shut-off valve must be provided with BMZ (emergency in case of fire alarm) | GxP, necessary |

Process requirements

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| URS# | Description | Classification |
| 4.2.5-1 | Constant volume flow at sampling points | GxP, necessary |
| 4.2.5-2 | At each point of collection, the same quality must be present at all times | GxP, necessary |
| 4.2.5-3 | The following process conditions shall be taken into account for PW. Pressure at the last customer shall be interpreted as 3 bar | GxP, necessary |

Functional requirements

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| URS# | Description | Classification |
| 4.2.6-1 | Calibration of sensors must be present | GxP, necessary |
| 4.2.6-2 | Monitoring of critical parameters: triggering of alarms Normal condition: no alarm over/underrunning: alarm (acoustic or optical) | GxP, necessary |
| 4.2.6-3 | Mode of operation: A fully automatic, continuous operation is to be guaranteed | GxP, necessary |
| 4.2.6-4 | The PW system must be sanitisable (e.g. 30 min / 80°C cycles with tolerance) | GxP, necessary |

Monitoring

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| URS# | Description | Classification |
| 4.2.7-1 | Monitoring of previously defined, critical Parameters | GxP, necessary |
| 4.2.7-2 | The system shall be capable of triggering alarms in case of GMP-relevant limit values. | GxP, necessary |
| 4.2.7-3 | An overview of maintenance and malfunction messages in the system shall be presented, including in particular alarm messages. | GxP, necessary |
| 4.2.7-4 | Documents and data must be easily accessible to users | GxP, necessary |
| 4.2.7-5 | Data (monitoring) is recorded and archived | GxP, necessary |
| 4.2.7-6 | Data must be protected from tampering by unauthorised persons (within the organisation as well as during transmission) | GxP, necessary |
| 4.2.7-7 | Data must be readable/reserved for the entire period of retention | GxP, necessary |
| 4.2.7-8 | PW monitoring Continuous monitoring of conductivity in feed and return Continuous monitoring of the TOC in return | GxP, necessary |
| 4.2.7-9 | PW storage temperature: 20 °C ± 2°C conductivity: see URS# 4.2.3.3-3 Sanitization temperature: ≥ 80°C Flow velocity: 2-4 m/s | GxP, necessary |

Requirements for security and access and authorisation controls

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| URS# | Description | Classification |
| 4.2.7.1 | Several security levels and audit trail need to be implemented | GxP, necessary |
| 4.2.7.1-1 | The system must be protected either by physical access control or by changing passwords | GxP, necessary |
| 4.2.7.1-2 | The system shall provide for several levels of security depending on the responsibilities of the user | GxP, necessary |
| 4.2.7.1-3 | The system must generate an audit trail | 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 enable backup and recovery functionality | 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 or other regulations | GxP, necessary |
| 4.2.7.3-2 | Electronic data is archived on an internal 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 | Security patches and updates are installed by the maintenance technician during inspection/maintenance according to previously agreed rules | GxP, necessary |

Documentation and training requirements

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| URS# | Description | Classification |
| 4.2.8 | The documentation shall be prepared in German and shall include all relevant lists and electrical documentation. | GxP, necessary |
| 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 | Uniform marking of all components and components in all documents | GxP, necessary |
| 4.2.8-4 | The version control of all manufacturer documents must be ensured by means of a change history | GxP, necessary |
| 4.2.8-5 | All documents must be available until acceptance (SAT) final | GxP, necessary |
| 4.2.8-6 | EC declaration of conformity for all components of the scope of delivery | GxP, necessary |
| 4.2.8-7 | CE marking | GxP, necessary |
| 4.2.8-8 | Initial calibration of the sensors | GxP, necessary |
| 4.2.8-9 | Function description | GxP, necessary |
| 4.2.8-10 | Recommendations/Guides incl. Manufacturer's schedules for maintenance/ Maintenance | GxP, necessary |
| 4.2.8-11 | Test certificates of welders and test personnel used | GxP, necessary |
| 4.2.8-12 | Endoscopic control of all hand-welded seams Not applicable to oxygen distribution | 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 | Wear Part List Excluding DL Distribution | 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 the system response) | GxP, necessary |
| 4.2.8.1-4 | Parameters list | GxP, necessary |
| 4.2.8.1-5 | Component List | GxP, necessary |
| 4.2.8.1-6 | List of measuring instruments | GxP, necessary |
| 4.2.8.1-7 | A measuring station plan shall be drawn up. | GxP, necessary |
| 4.2.8.1-8 | A calibration list for relevant measuring points with description and acceptance criteria shall be drawn up. | GxP, necessary |
| 4.2.8.1-9 | A maintenance specification list shall be created. | GxP, necessary |

Electrical documentation

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| URS# | Description | Classification |
| 4.2.8.2-1 | Create a cable list | GxP, necessary |
| 4.2.8.2-2 | A schematic must be available in "as-built" version | GxP, necessary |
| 4.2.8.2-3 | Certificate of compliance with safety requirements (CE-conformity for control cabinet) | GxP, necessary |

Operator documentation

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| --- | --- | --- |
| URS# | Description | Classification |
| 4.2.8.3-1 | Logbooks must be present or, if necessary, created | GxP, necessary |
| 4.2.8.3-2 | Technical data sheets or manuals must be provided (including sensors) | GxP, necessary |
| 4.2.8.3-3 | Instructions for operation/safeguarding/maintenance of the media (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 | GxP, necessary |
| 4.2.8.4-3 | Certificates Surface roughness | GxP, necessary |
| 4.2.8.4-4 | Welding report, welding protocol | GxP, necessary |
| 4.2.8.4-5 | Assembly test report/ Certificate of acceptance | GxP, necessary |
| 4.2.8.4-6 | Execution of a pressure sample | GxP, necessary |
| 4.2.8.4-7 | Filter certificate (level of separation and suitability) | 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\_GEB\_O2GMP Relevance analysis Oxygen

GMP-I\_GRA\_GEB\_DLGMP Relevance analysis of compressed air

GMP-I\_GRA\_GEB\_PWGMPRelevance analysisPW

21 CFRTitle 21 of Code of Federal Regulations

COMMUNICATIONpharmacovigilance and active substance manufacturing regulation

EU GMP Part IIBasicrequirementsforactiveSubstancesuseded

andAnnicesstartingmaterials

Annexes

GMP- No, no, no, no, no, no, no.I\_Media\_URSA1Me-service connections

GMP-I\_Media\_URSA2Block flow pattern PW Production and distribution