Installation Requirement Specification and Specific Instructions

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1.0 Approval Signatures

This document is prepared by the Process, Validation and GMP Compliance team of "NNE Pharmaplan India" for the project "Integrated Vaccine Complex, Chengalpattu, Chennai" (**project number:** 120310) of HLL BIOTECH LIMITED (Chennai) under the authority of their Project Manager. Hence, this document before being effective shall be approved by the QA team of HLL BIOTECH LIMITED, and authorized by the appropriate Project Authority.

NNE Pharmaplan India Ltd				
Responsibility	**Name**	**Designation**	**Sign**	**Date**
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Engineering/Projects				
Production				
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COO				

Specifications	Remarks
2.0 Overview	
2.1 Project Introduction	
HLL Biotech Limited (HBL), a subsidiary of HLL Lifecare Limited, (a CPSU under Ministry of Health & Family Welfare, Government of India, is implementing "Integrated Vaccines complex" Chengalpattu. The proposed complex is a state of the art facility with cGMP compliance for manufacturing vaccines required for the immunization programme of Government of India. HLL Biotech Limited has associated with NNE Pharmaplan India Limited, hereinafter called as "NP" has been appointed as "Engineering Consultants". NNE Pharmaplan shall design and engineer this facility, incorporating the latest GMP Standards and best practices. This facility shall be built as per the latest International trends and upon completion, shall be in compliance with Indian FDA (Schedule M), WHO/GMP regulations.	
2.2 Project Standard	
The facilities, upon completion, shall be in compliance with the Indian FDA (Schedule M), WHO, and also the HBL's internal quality standards.	
2.3 Purpose	
This specification states the mandatory requirements and critical instructions for process systems, process support systems and utility systems.	
3.0 Scope	
3.1 **Systems in scope**	
The specification applies to process systems, process support systems and utility systems used for producing vaccines. For each requirement (see section 5.0 "Requirement specification"), it is more explicitly specified what types of systems the requirements apply to. The specification applies both to new systems and to changes of existing systems (if applicable and then only to the parts that are changed). HVAC systems, automation and electrical building installations are not included in the scope.	
3.2 **Supplementary or changed requirements**	
The specification covers mandatory requirements and critical instructions. There may be cases when more specific requirements than described in this specification are necessary. It may be supplementary requirements; In such cases, the User Requirement Specification (URS) must state which requirements are applicable and where precisely deviations are made from this instruction	
3.3 **Note**	
"**Vendor** is required to adhere to all necessary and applicable requirements. Any specific requirement not applicable should be mentioned in the remark column. Also, any deviation or non-compliance a comment must be inserted or enclosed as a separate	

Specifications	Remarks
annexure by referring to the respective IRS specification number." For more information vendor to refer Tender enquiry document no: NPI-120310-EQP-TD-S1-01.	
4.0 Safety Requirement	
4.1 **General**	
Following facilities must be provided to protect personnel, product and equipment / system:	
4.1.1 In the event of equipment / system malfunction or loss of utilities, the unit must contain all necessary protection devices to ensure that the equipment / system and the article remain in a safe condition.	
4.1.2 Noise level <75 db at a distance of 1 meter from the equipment / system.	
4.1.3 Emergency stop switch should be located on accessible areas or within the reach of the operator and a signal has to display when emergency stop button was activated..	
4.1.4 Earthing all parts of the machine, including doors, movable units etc to the earth grid/cable/tag box, supplied by the electrical contractor	
4.1.5 In case of power failure, the system must be protected in the following priority and the likeliness of damages must be minimized: • Persons and environment • Equipment • Product	
4.1.6 For the safety of the operator the external surfaces should not have temperature more than 45℃.	
4.1.7 Warning stickers on all hot surfaces	
4.1.8 Appropriate closure of all rotating parts of machine.	
4.1.9 Appropriate failure detection and alarm notification	
4.1.10 All machine doors which are closed during production, according to operator safety, have to be supervised by security switches. In case of door opening the machine must stop immediately.	
4.1.11 Explosion proof design.	
4.1.12 Motor fault or over load.	
4.1.13 Sufficient lighting inside machine housing and control cabinets must be provided by the vendor.	
4.1.14 Vibrations shall not exceed level acceptable according ISO 10816.	

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4.1.15	All lines and equipment surfaces which represent a danger to operators and maintenance personnel with regard to freezing or burns will be adequately insulated.	
4.1.16	Generally all sensors are supplied via the uninterruptible network. Thus the actual system condition can be displayed even in case of voltage failure.	
4.1.17	Control lights and other display elements shall not be influenced by voltage failure.	
4.1.18	Grounding of the entire framework is required	
4.1.19	All motors have to be thermally protected	
4.1.20	The level of protection of the electrical components has to be IP54 or higher based on the Process requirements.	
4.1.21	Audio alarms have to be in the range of 2.3 — 2.9 kHz in order to avoid interference and confusion with evacuation alarms.	
4.1.22	As per the state electricity board, harmonics for all electrical wiring should remain within 3%. Active or passive filters should be used. The same has to be clearly marked in circuit diagrams. Detailed information to be provided in spare lists etc	
4.2	**Power Failure and Recovery**	
4.2.1	On power failure equipment shall come to rest to protect operator, equipment and the product.	
4.2.2	After power resumption, the machine should not start automatically i.e. human intervention should be required.	
4.2.3	After power regain, the machine should start from the step it stopped with the provision of real time recording and printing facility.	
5.0	**Requirement specification**	
5.1	**Refrence Standard / Guideline for Equipment / System**	

The equipment should comply with the following guidelines / standard:

Sl. No.	Reference Standard / Guideline	Applicability
1.	**Current GMP-Regulations** • EU-GMP-Guideline Part 1, Annexes 1, 11 & 15Schedule “M” GMP • 21 CFR, Part 210 cGMP in Manufacturing, processing, packing or holding of drugs: General • 21 CFR Part 211: Current Good Manufacturing Practice for finished Pharmaceuticals • WHO Good Manufacturing Practices - Main	General requirement for all the equipments / systems (pharmaceuticals/biologics/vaccines)

Specifications	Remarks

	Principles for Pharmaceuticals Products • WHO Good Manufacturing Practices for biological products **Operating safety act** • The requirements of the Operating safety act must be observed. **ASME-BPE compliance** • ASTM, American Society of Testing Materials • ANSI, American National Standard Institute • AWS, American Welding Society	

Sl. No.	Reference Standard / Guideline	Applicability
2.	**FDA Guidance for Industry** Sterile Drug Products Produced by Aseptic Processing-cGMP	For all equipments/systems used in aseptic manufacturing
3.	**FDA Guidance for Industry** Documentation for Sterilization Process Validation in application for human and veterinary drug products	For equipments used in sterilization such as autoclave / DHS etc
4.	**GAMP** The Good Automated Manufacturing Practice (GAMP) Guide for Validation of Automated Systems in Pharmaceutical Manufacture, Vol. 5 **Current GMP-Regulations** 21 CFR Part 11: Electronic Records; Electronic Signatures	For automated / semi – automated computerized systems
5.	**CE Conformity** A CE declaration of conformity must be available. The CE identification must comply with the current EC commission	For products placed on the market in the European Economic Area (EEA) (all the systems / equipments).
6.	**ASME** Section 8- Div I for pressure vessels design ASME-BPE Compliance (As per latest version)	For all pressure vessels / reactors / fermentors / autoclave / sterilizers etc
7.	**ANSI / NSF 49-2008** Biosafety Cabinetry : Design, Construction, Performance and Field Certification	Biosafety cabinet
8.	**ISO 14664** Clean Rooms and its Associated Controlled Environment **(European Standard) EN – 1822 for HEPA**	Any equipments with HEPA filters (RABS / LAF / BSC etc)

Specifications			Remarks
	FILTERS		
9.	**ISO 8362** Injection containers for injectables and accessories	For Vials and closures	

5.2	**Cleaning Requirement**	
5.2.1	Design of equipment should be smooth to enhance cleaning feasibility and by providing zero sharp corners, crevices and smooth weld joints.	
5.2.2	All bolts, nuts on the exterior part of equipment will be with cap head or cap nut	
5.2.3	The vendor shall provide the detail of cleaning agent based on compatibility of material.	
5.2.4	Equipment contact parts shall be easily dismantle-able and cleanable	
5.2.5	The equipment shall be easily accessible for cleaning of non-product contact part at maintenance side of the system	
5.2.6	All gaskets provided to avoid leakage should be able for easy removal & re- fixing.	
5.2.7	The vendor shall provide the detail of utilities requirement for the applicable cleaning (WIP / CIP / SIP).	
5.2.8	Systems with CIP shall be designed for 100% coverage of the internal surface areas.	
5.3	**Qualification Requirement**	
5.3.1	Equipment shall be qualified for design phase (DQ), installation phase (IQ), Operational phase (OQ) and the performance phase (PQ). Computer system verification as per the standards of GAMP.	
5.3.2	Vendor shall support and provide all necessary documents and test procedures to client for proper execution of all the qualification phases.	
5.4	**Material of Construction (MOC)**	
5.4.1	Materials:	
	Materials: Surfaces in contact with media must be of a material quality which does not react with to, absorb, leach or contaminate the media to an extent that will impact the product quality. The materials specified in row must always be evaluated in relation to the specific media that the material will get in contact with. Particular limitations regarding the use of materials shall be specified in the respective URS.	
	Acid-proof stainless steel, resistance: Many types of acid-proof stainless steel are not	

Specifications	Remarks
sufficiently resistant to media with low pH (under ~3) or high chloride content, particularly HCl solutions. Where acid-proof stainless steel is not sufficiently resistant PP, PE, PVDF or PTFE are recommended.	
Declaration of Compliance: Materials of construction must as a minimum be documented with a Declaration of Compliance from the supplier. The Declaration must contain a guarantee that the used/supplied materials are in compliance with the specified/ordered. Suppliers of pipes, fittings, components, instruments and systems must be able to trace the materials to the material manufacturer's "heat number" and the material composition of the specific batch. The supplier's ability to secure this traceability can for instance be ensured via supervision, audit and performance history as part of the approval of the supplier.	
Specifications:	
• All metallic product contact / critical surfaces should be constructed of SS316 L grade with internal mirror finish (< 0.5µ Ra for filling line and < 0.8µ Ra for lyophiliser) and external surface matte finish (< 1.2µ Ra).	
• All metallic non-product / noncontact / non critical surfaces should be constructed of SS304 grade or better (316 in sterile area) with external surface finish as matte finish (< 1.2µ Ra).	
• Gaskets, seals and O-rings coming in direct / indirect contact surfaces should be constructed of USFDA approved polymeric materials only.	
• Borosilicate glass should be used wherever required eg:- inspection door viewing port in the machine etc.	
• Material of insulation shall be mineral wool/ ceramic wool cladded with SS 304.	
Area of application: The requirements apply to process systems and clean utilities. For other systems the requirements are intended as guidance and are in such cases not subject to formal tests.	

Alternative materials listed below.
• **Acid-proof stainless steel** with content of
  ○ Molybdenum ≥2.0% and Carbon ≤ 0.03%.
• *For example: AISI 316L, AISI 904L, EN1.4404, EN1.4435, EN1.4462,*
• *EN1.4539, UNS S32205, others.*
• Also accepted: AISI 316Ti and EN1.4571.
• If the material is not to be welded, accepted are also:
  ○ Molybdenum ≥ 2.0% and Carbon ≤ 0.08%.
• *For example: AISI 316, EN1.4401, others.*
• **Polymers**, accepted types:
• CSM (Hypalon), E-CTFE, EPDM/EPD, FEP, FFKM, FPM (Viton), PE, PEEK,
• PFA, PP, PTFE (Teflon), PVDF, SI.
• In LPLC columns: acrylic	

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• In addition, the material must comply with 21 CFR part 177 or USP 24 Class VI. • **Liquids** must comply with 21 CFR part 172 or part 178. • *By "liquids in contact with media" is here understood lubricants and other liquids in equipment, components and instruments where there is a high probability of direct contact with the medium by wear and tear, defects, failures, etc.* • **Other materials**, accepted types: ○ Titanium *e.g. EN3.7025, EN3.7035, EN3.7235* ○ Hastelloy *e.g. C4, C22, C276* ○ Ceramics *e.g. alumina, zirconia* ○ Glass*e.g. borosilicate* ○ In mechanical seals and the like, also SiC and WC.	
5.4.2 **Untreated welds**	
Welds: Untreated welds in contact with media must have a sanitary finish. This facilitates easy and effective cleaning and minimise the risk of corrosion, microbial growth and other contamination of the product. For treated (burnished, polished) welds in stainless steel, Plastic welds are not treated.	
100% inspection of all welds is not required. The quality of the welds is instead secured through a number of indirect requirements and spot checks and welder qualification.	
Few welds: In cases when only a few welds are to be carried out, a 100% independent inspection can be chosen instead of the 5% stated in requirement a) In that case, requirements on certificates (b,2) and 20% self-inspection (b,4) are cancelled.	
Self-inspection: By self-inspection is meant an inspection that is carried out by the welding contractor's inspection function.	
Independent inspection: By independent inspection is meant an inspection carried out by a Technical Discipline Specialist who is organisationally independent from the welder. It is recommended to use Technical Discipline Specialists from a organisation with accreditation to perform welding inspections.	
Extended inspection: If the inspection uncovers welding defects or discolorations, the inspection must be extended to determine the extent of the problems (for instance by systematic inspection of the specific welder's work).	
Pickling: For welds in stainless steel there may be cases where it is very difficult to achieve welds without too much discoloration. In such cases, pickling or passivation is acceptable, but it is not recommended as a general procedure.	
Specifications:	
• All welds shall be crack and crevice free.	
• Internal welds and welds likely to be in contact with the product shall be ground smooth and flush. All other welds shall be ground smooth (< 1.2µ Ra).	

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• Clean media pipes shall be orbital welded	
• All welds shall be polished to the same standard as the surrounding areas, with direction of lay following the direction of welding.	
• Insulation material should be non-fibrous and covered with completely welded SS 304 or better cladding.	
• Stainless steel fabrications must be welded under inert gas (Orbital welding) with Boroscopy records and treated by pickling and passivation to pharmaceutically accepted standards, to prevent corrosion.	
Area of application: The requirements apply to process systems. For systems with dry gases there are however no requirement for independent inspection (part of requirement a), and the requirement is verified by commissioning. For other systems the requirements are intended as guidance and are in such cases not subject to formal tests.	
a] Untreated welds in stainless steel in contact with media must be without welding defects – as defined in [ASME BPE, MJ-6] or equivalent standard. Discoloration exceeding ”light straw” or ”light blue” must not exist in the heat-affected zone (cf. [AWS], [Force] or equivalent standard). At least 5% of a system’s welds must be inspected for discoloration and welding defects by an independent Technical Discipline Specialist. The inspection must be targeted the welds that the independent Technical Discipline Specialist considers hardest to make error-free and the inspection must representatively be spread on the welders. The inspection must be carried out using boroscopy, endoscopy or direct visual inspection.	
b] Untreated welds in stainless steel in contact with media must be: 1. Traceable to welder, welding procedure and self-inspection via a welding log. 2. Made by welders holding a valid welding certificate to weld in the specific materials and dimensions. The certificate must be issued by an accredited authority *(for example Force Technology and others)*. 3. Executed according to an approved welding procedure (WPS). 4. Self-inspected by sampling for welding defects and discoloration (cf. req. a). The inspection must be carried out using boroscopy, endoscopy or direct visual inspection. The self-inspection must be carried out on at least 20% of the welds. The inspection must be targeted the welds which the construction supervision staff considers hardest to make error-free and the inspection must be representatively spread on the welders.	
c] Welds in thermoplastics, in contact with media must be 1. Without welding defects - as defined in [ASME BPE, PM-3.4.1] or equivalent standard. 2. Made by fusion welding with a machine where data for critical welding parameters is recorded automatically. 3. ”Beadless butt fusion” type welds in systems with formal requirements to drain ability (see section title "drain-ability).	

Specifications		Remarks
	4. Traceable to welder, welding procedure and welding data via a welding log. 5. Made by welders who hold a valid welding certificate to weld the specific materials. The certificate must be issued by an accredited authority, alternatively an authority approved by the material supplier. 6. Executed according to an approved welding procedure (WPS).	
5.5	**Use of Lubricants**	
5.5.1	Any lubricant, if used in the equipment / system must be of food grade and non-toxic.	
5.5.2	If lubricant use, All lubricating points must be clearly shown and labeled.	
5.6	**21 CFR Part 11 Compliance**	
5.6.1	Automation and Human Machine Interface (HMI); the software/Hardware system should generate data that cannot be manipulated by the operator. Compliance to 21CFR part 11.	
5.6.2	Vendor to perform a criticality assessment to assess the applicability of the system to Part 11 regulation. Software if used to generate, process, store the critical data must be validated and must be upgradeable to 21 CFR Part 11 requirements.	
5.6.3	The vendor may be also allowed to use CAT6 or CAT6a cables,(RJ-45) cables to do communication	
5.6.4	RS 232 interface is required to transfer the data and as well to take the printout.	
5.6.5	A backup of the data must be available on the system, locked and not tampered by the operator. The data must not be able to manipulated by the operator.	
5.6.6	The audit trail for the data integrity may need to include functions such as authorized user, creations, links, embedded comments, deletions, modifications/corrections, authorities, privileges, time and date etc.	
5.6.7	**Area of application:** This requirements apply to all types of critical process equipments and utility systems (such as BMS of HVAC, PW, WFI & PSG) with HMI, PLC / Software	
5.7	**Data Integrity**	
5.7.1	System security shall be provided to access the operation system and to alter configurable parameter values through access password.	
5.7.2	Minimum 3 level password shall be provided as: • **Operator:** Shall provide operator access to allow routine operation of all equipment features • **Supervisor:** Shall provide access to operator level features in addition to critical operating parameter configuration • **System Administrator:** Shall provide the access to the Operator and Supervisor level features in addition to system security parameters.	

Specifications	Remarks
5.7.3 **Area of application:** This requirements apply to all types of critical process equipments and utility systems (such as BMS of HVAC, PW, WFI & PSG) with HMI	
5.8 **Batch Data Display and Record Printing**	
5.8.1 **A complete batch display indicating the following important parameters, but not limited to these:**	
5.8.1.1 Start date and time of operation	
5.8.1.2 End date and time of operation	
5.8.1.3 Product name and Batch No (For process equipments)	
5.8.1.4 All failures alarms (/repeated alarm) and notification	
5.8.1.5 Operator code and name	
5.8.1.6 All process parameters	
5.8.2 **A batch record indicating the following important parameters but not limited to these**	
5.8.2.1 Product name and Batch No (For process equipments)	
5.8.2.2 Start date and time of operation	
5.8.2.3 End date and time of operation	
5.8.2.4 All failures alarms (/repeated alarm) and notification	
5.8.2.5 Operator code and name	
5.8.2.6 Adequate space for writing remarks / corrective actions if any.	
5.8.2.7 Identified space to sign for operator & supervisor.	
5.8.3 **Area of application:** This requirements apply to all types of critical process equipments and utility systems such as PW, WFI & PSG	
5.9 **Desired Documents**	
5.9.1 Vendor must generate all applicable documents during all phases of equipment fabrication i.e. design fabrication, testing and shipment as per applicable standards.	
5.9.2 Following documents, but not limited to these, are expected from the vendor as part of the supply package as hard copy (02 No.) and electronic editable versions in **English** language:	
5.9.3 **Phase 1: Pre-ordering of the equipment**	

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5.9.3.1 Filled in URS	
5.9.3.2 Equipment layout drawing fitted in the room layout block	
5.9.3.3 Detail technical offer that support the compliance of the URS must include the make of the components and P&ID Proposal.	
5.9.4 **Phase 2: Post-ordering and pre-fabrication stage of the equipment**	
5.9.4.1 Functional design specification and technical specification, that should contain the following:	
5.9.4.1.1 Equipment descriptions and its function	
5.9.4.1.2 Equipment operation steps	
5.9.4.1.3 HMI functions with screen shot	
5.9.4.1.4 List of failure indications	
5.9.4.1.5 List of interlocks	
5.9.4.1.6 List of input/outputs and its functions	
5.9.4.1.7 Critical list of major component, devices and instruments with their specific functions, specifications data sheet	
5.9.4.1.8 Schematic/GA drawings of the equipment.	
5.9.4.1.9 List of article contact surface and its MOC	
5.9.4.2 Based on the above documents, equipment design shall be evaluated and approved by the user for the fabrication.	
5.9.5 **Phase 3: Fabrication stage of the equipment & FAT**	
5.9.5.1 Vendor shall provide the Factory Acceptance Test (FAT) protocol at least 4 weeks in advance of the date of FAT, for the approval by the user.	
5.9.5.2 Internal FAT reports compiled by vendor should be shared with the client for reference.	
5.9.5.3 Vendor shall arrange the necessary raw materials (vials, rubber bungs etc) to demonstrate the following tests like productivity, synchronization etc	
5.9.6 **Phase 4: Delivery of the equipment & SAT**	
Delivery of the Equipment:	
5.9.6.1 Vendor shall provide the following documents in the delivery package in minimum 2 sets. The delivery package shall reach the site of user at least 15 days before the delivery equipments for the engineering check of the documents.	

Specifications		Remarks
5.9.6.2	Operation and maintenance manuals, preventive maintenance schedule (with recommended consumables and recommended time interval) for equipment's major component as well as the operating system	
5.9.6.3	Operation and maintenance manuals for the bought out items.	
5.9.6.4	Installation instructions/ guideline for equipment	
5.9.6.5	Final as-built drawing for equipment.	
5.9.6.6	Detailed drawing (plan and minimum one elevation) marking clearly all the necessary dimensions and locations of utilities along with requirement of utilities on the drawing along with the offer.	
5.9.6.7	Other applicable drawings (such as P&ID, electrical, instrumentation etc.)	
5.9.6.8	Spare and/ or change parts list with ordering information	
5.9.6.9	MOC certificates for all direct/ indirect product contact surfaces.	
5.9.6.10	Detailed description of all components with the manufacturer name, code/sr. no., function, MOC, different test reports, manuals with the installation guideline of different components (as applicable) etc.	
5.9.6.11	Equipment, components, valves and instrumentation etc. shall be uniquely identified by some code / numbering system and the same shall be shown in Process & Instrumentation (P&I) and General Arrangement (GA) drawings.	
5.9.6.12	Instrument calibration certificates with respect to the traceable national reference standard instrument and their calibration procedure. Original calibration certificate along with traceability to be submitted by vendor in their IQ file.	
5.9.6.13	Different reports like Welding, Boroscopy, Passivation etc. (whichever is applicable)	
5.9.6.14	Recommended SOPs for operation (Start-up and shutdown), general cleaning and maintenance of each equipment	
5.9.6.15	Guarantee/ warranty certificates for each equipment and major bought-out items, such as PLC, printer, recorders, instrumentation etc.	
5.9.6.16	Software installation CD with 2 back-ups, wherever applicable.	
5.9.6.17	Software recovery procedures in case of computer system breakdown, for equipment control system, wherever applicable.	
5.9.6.18	Vendor must generate and provide all specifications and test certificates of software used in the equipment control and/or monitoring system.	
5.9.6.19	Shipping checklist along with size & gross weight of each equipment	

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5.9.6.20 IQ and OQ protocols	
5.9.6.21 Control System input / output verification data and report (Optional)	
5.9.6.22 Types of Lubricant and Lubrication instructions. Food grade certificate	
Documentation & Drawing Requirement	
5.9.6.23 All documents have to be supplied as Hard copy, PDF and native file (doc, xls, ppt, dwg, etc.).	
5.9.6.24 All documents have to be archived in DIN A4 binders. Larger formats have to be folded according to the requirement.	
5.9.6.25 Each binder must be marked with the binder number and number of binders.	
5.9.6.26 Different documents within a binder must be separated by extra separator sheets	
5.9.6.27 A Table of content is necessary for the whole documentation.	
5.9.6.28 User manual: Descriptions and manuals must contain all necessary information about safety, installation, commissioning, operation, maintenance and troubleshooting.	
5.9.6.29 If an initial calibration will be not carried out, at least a manufacture's calibration certificate must be delivered.	
5.9.6.30 Software back-up copies must be delivered for all used programmes to restore the system or software status quo ante.	
5.9.6.31 The drawing or document number must be clearly identifiable.	
5.9.6.32 Author/date of creation and reviewer/date of review have to be listed on each drawing, plan and diagram.	
5.9.6.33 The scale must be declared.	
5.9.6.34 The size and format of the drawings, plans and diagrams have to be selected in such a way that all information is readable.	
5.9.6.35 All drawings and diagrams must be supplied in AutoCAD compatible formats.	
5.9.6.36 A legend including a clear designation must be issued for all used symbols.	
5.9.6.37 Appropriate block diagrams must be developed in case of complex equipment.	
5.9.6.38 The process flow inside of the equipment must be displayed in a clear and balanced manner e.g. with arrows and text.	
5.9.6.39 The flow directions of the media must be displayed in the drawing.	

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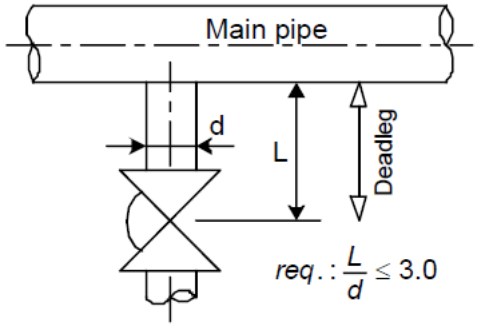
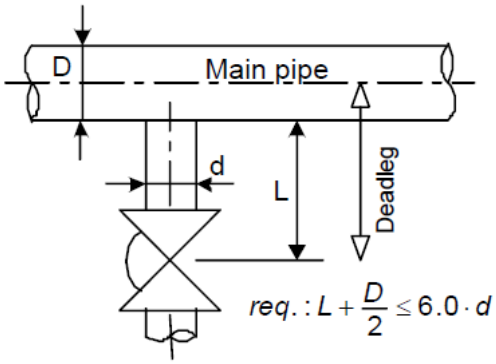
5.9.6.40	Main dimension and all dimensions of connections to other systems must be indicated.	
5.9.6.41	Equipment with the requirement of drainability must be indicated with slope and direction of slope.	
5.9.6.42	Software ladder logic/ operation and controls flow charts	
5.9.6.43	Biological compatibility certificates of all non metallic parts	
5.9.6.44	The vendor to work out a list showing all documents included in his scope of work and delivery.	
5.9.6.45	All documents require a document control Section listing all versions and indicating executed modifications.	
5.9.6.46	Delivered software must be forwarded on suitable Storage medium in a format suitable for installation. Source codes for Client specific applications must be handed over as electronic files.	
5.9.6.47	If cables have to be pulled by third parties, cable lists with following information are required: unique cable ID-No, cable type, start and endpoint, differentiation between power and control cable, particular requirements.	
5.9.6.48	If the equipment has a control system, all PLC components like I/O-cards and local units like bus nodes, valve terminals or control panel must be listed with information at least about tag name, description, type, vendor's item number and a reference to the appropriate manual with the installation guideline.	
5.9.6.49	Other components next to the PLC like frequency converter, servo controller, electronic cams, transmitter, etc. all single items must be listed with information at least about tag name, description, type, manufacture, and a reference to the appropriate manual books with the installation guideline.	
5.9.6.50	If the equipment contains PCs, the performance data of the PC with processor type/manufacture/tact frequency/hard disk size and RAM must be labeled. Peripheral apparatus like I/O-cards, graphic cards, etc. which do not operate with standard drivers must be indicated and must also be contained information at least about the description, type, manufacture and a reference to the appropriate manual books with the installation guideline.	
5.9.6.51	Supplementing the P&I diagram: A valve position matrix must be developed for complex processes. The conditions of valves and engines must be described in the various process steps.	
5.9.6.52	If the plant is equipped with a PLC, a print of the programming environment must be generated and printed.	
5.9.6.53	Calibration certificate should have validity of at least 12 months from the date of installation	

Specifications	Remarks
5.10 Training Requirement & Support	
5.10.1 A special training for operators, supervisor, and maintenance, electrician staff (min. 5 days each) has to be included in the offer.	
5.10.2 Training must be carried out by qualified personnel. Training documents must be handed over to each participant at the beginning of the training. A training certificate describing the training subjects must be worked out.	
5.10.3 Training documentation to be issued for operator's easy handling and error analysis.	
5.10.4 The Vendor shall provide start-up services through successful completion of the site acceptance test. The site acceptance test will be a repeat of the factory integration test performed at the Vendor's facility.	
5.10.5 The Vendor shall provide a four (at least 4) hour training course to twelve (12) maintenance people on troubleshooting and repair of the system.	
5.10.6 A concise operating instruction shall be issued containing e. g. pictures for operator's easy understanding of the process.	
5.10.7 Maintenance to be carried out must be clearly and plainly described. Description of the maintenance of all components to be summarized in one document.	
5.10.8 Vendor should specify the in-house strength / capabilities and offer to support for the process validation and optimization of the actual process cycle.	
5.10.9 The Vendor shall provide a twenty-four (24) hour technical support phone number with a maximum of thirty (30) minute response time to calls requesting assistance. Support personnel for this hotline must be knowledgeable and professional.	
5.11 GMP Requirement	
5.11.1 A clear separation between clean and technical area must be realized.	
5.11.2 All utility line shall be properly identified with direction	
5.11.3 All drives, filters, pumps, valves (specially chamber drain) should have easy access	
5.11.4 The sterile filters must be testable for integrity. Vendor should provide the certification with Test procedure for Integrity and no of sterilization cycle in the Certificate.	
5.11.5 For all clean media a sampling valve should be provided at supply and in drain. Sampling valve should be certified 1.5D requirement for Dead leg.	
5.11.6 An appropriate seal must be used for connecting the paneling to the suspended ceiling, clean room walls and floor.	
5.11.7 The front paneling of the system installed in clean room must be gas tight to the technical area of the system	

Specifications	Remarks
5.11.8 The bio-seal provided for aseptic area equipment should be air tight.	
5.11.9 **P&ID Diagram**	
P&I diagrams: are the basis for detailed design, correct functionality, process understanding, maintenance and tracing of the components and instruments in a system. P&I diagrams must therefore be available that have each single component and instrument unambiguously defined by a tag. The plant must be verified to be constructed according to the P&I diagrams and they must subsequently be maintained "as built".	
Components: Every tagged component/instrument on the P&I diagrams must be registered (in databases or lists) with information that supports correct maintenance. Relevant information includes: manufacturer, type, model, dimensions and materials of construction.	
Data sheet, Maintenance instruction: A data sheet and maintenance instructions must be available for each component/instrument type (can be combined in one document).	
Tamper proof Tag numbers: Marking of tags must be executed in a quality that secures durability and resistance to the environment where they are placed (for example temperature, humidity, sunlight).	
Specification:	
• Upon equipment delivery, Vendor shall supply client with a register containing all details of component numbers issued.	
Area of application • Pipes must be laid out according to P&I-diagram. • Where slope on pipes are marked on the P&I diagram, slope must be established with the indicated direction. • Where drainage to drain systems is marked on the P&I diagram, air break must be established. • Placement of components and instruments must be mutually correct according to the P&I diagram. • Components and instruments must be marked with the tag shown on the P&I diagram. • Components and instruments must be drawn on the P&I diagram with the correct symbol. • Components and instruments must be registered on component/instrument lists with correct tag, type and manufacturer.	
Component and instrument databases (or lists) must, for each component / instrument, contain data for • Type • Manufacturer • Model • Dimensions • Materials of construction For each component / instrument type, a datasheet and maintenance instructions must be available.	

Specifications	Remarks
5.11.10 **Sanitary components**	
Sanitory Components: All process equipment (including couplings, fittings and clamps) in contact with non-bacteriostatic media must be of a sanitary type. This facilitates easy and effective cleaning and minimise the risks of microbial growth and other contamination of the product. Whether the equipment can be considered to be sanitary must be assessed based on international, accepted standards for sanitary designs, for example EHEDG Guidelines, 3-A Sanitary Standards or ASME's Bioprocessing Equipment [ASME BPE].	
Specification:	
• All valve and fitting in contact with the media shall be of sanitary type and suitable for aseptic use	
Area of application: The requirements apply to process systems. The requirements are however not relevant to: • Systems with dry gasses. • Self-draining pipe branches in systems with pure steam. a] Tanks, centrifuges, pumps and other process equipment, as well as components and instruments, must be of a sanitary type. b] Couplings, fittings and clamps must be of a sanitary type.	
5.11.11 **Prevention of cross-contamination**	
Cross Contamination: Process systems must be designed so that the risk of cross-contamination is minimised between media that must not get in contact with each other. Prevention against cross-contamination through leaking valves must always be established between CIP systems and other media and always between water systems and other media". Whether the systems must be secured against leaking valves between other media one to another is assessed individually and must be stated in the system's URS or other requirement specifications, and must also be reflected in the design solution.	
Double Block and Bleed: Process systems must be designed so that the risk of cross-contamination is minimised between media that must not get in contact with each other. Prevention against cross-contamination through leaking valves must always be established between CIP systems and other media and always between water systems and other media". Whether the systems must be secured against leaking valves between other media one to another is assessed individually and must be stated in the system's URS or other requirement specifications, and must also be reflected in the design solution.	
Heat exchangers:	

Specifications	Remarks
Heat exchangers must be of the type double-plated heat exchanger or double tube-sheet tubular heat exchanger (Ref section title "sanitary components"), where leaks are detectable on the outside.	
Air break: Drainage towards drains must be secured against reverse suction and contamination with air breaks. Alternatively, a suitable sanitary mechanical device may be used, if the drain connection needs to be closed.	
Area of application: a] The requirements only apply to process systems. Design solutions must be chosen that prevent cross-contamination through leaking valves • Between CIP systems and other media • Between water systems and other media • Between other media one to another if specified in the URS or similar specifications. b] ”Air breaks” towards drain must be visible and at least 25 mm. c] Heat exchangers must be of the type double-plated heat exchanger or double tube-sheet tubular heat exchanger.	
5.11.12 **Deadlegs**	
Deadlegs: The incidence of "deadlegs" in process systems must be minimised to the extent possible to facilitate easy and effective cleaning and minimise the risk of microbial growth and other contamination of the product.	
Design: The design should aim at including as few deadlegs as possible. The deadlegs that cannot be avoided must be designed and constructed to be as small as possible. Deadlegs can result in a "hardest-to-clean area" which must be addressed in the cleaning validation.	
Area of application: The requirement applies to process systems. The requirement is however not relevant to: • Systems with dry gasses. • Dedicated systems with bacteriostatic media. • Self-draining pipe branches in systems with pure steam. a] For deadlegs, one of the acceptance criteria listed below must be fulfilled. As a primary rule, acceptance criterion 1 must be fulfilled. **Acceptance criterion 1** The length (L) of the branch measured from the outer surface of the	

Specifications	Remarks
main pipe must be smaller than or equal to 3.0 x the outer diameter (d) of the branch pipe. I.e.: L/d ≤ 3.0  **Acceptance criterion 2** The length (L) of the branch + the radius of the main pipe (half of the outer diameter, D/2) must be smaller than or equal to 6.0 x the outer diameter (d) of the branch pipe. I.e.: (L+D/2)/d ≤ 6.0  **Acceptance criterion 3** For diaphragm valves ≤ DN 10: The branch (deadleg) must be as small as possible (fulfilment of acceptance criterion 1 or 2 can't be expected).	
5.11.13 **Drain ability:**	
Drain ability: Process systems must be constructed so that they can be drained in connection with cleaning, maintenance and – if relevant – product or media changeover. Pipes must have slope. Components and instruments must be installed so that they are self-draining. For the lowest positioned points in the system ("local minima") a drainage arrangement must be built in, for example drain valve, clamp, pump connection, drain with "air break" or similar.	
Design: Short pipe sections should preferably be designed with a 2% slope and long pipe sections should be designed with a 1% slope. Slopes below 0.5% can only be	

Specifications	Remarks
accepted in exceptional cases.	
Specification:	
• All drains should be at the lowest point of the system for complete drainage.	
• The system shall have sufficient slope to drain out itself completely.	
• All utility pipes specifically pure steam/ water for injection/ condensate should have sufficient slope towards drain for complete emptying of the pipes	
• All drains must be equipped with an air-gap before connected to the drain system on site	
Area of application: The requirements apply to process systems. The requirements are however not relevant to systems with dry gases. Process support systems, utility systems and dedicated process systems with bacteriostatic media must all be drainable to allow easy and safe maintenance, but there is no requirement for a specific slope and the requirements are not subject to formal testing for these systems. **a]** Piping must have at least 0.5 % slope towards drainage points. There must be one or more points through which the piping can be emptied. **b]** The lowest positioned points in the system must all have a drainage possibility. Tanks and other process equipment, as well as instruments and components, must be designed and installed so the system can be drained. This includes that diaphragm valves on horizontal pipe sections must be angled in accordance with the valve manufacturer's instructions (if they cannot otherwise be drained).	
5.11.14 **Decontamination:**	
All surfaces in contact with media must be decontaminated (cleaned) before used in operation. This applies both to systems that are cleaned/CIP'ed as part of normal operations and systems that are not cleaned in operation. Decontamination should remove any contamination generated in connection with fabrication and installation of equipment, etc. The decontamination should not be confused with the cleaning that must be carried out in connection with the daily production. Decontamination does not necessarily ensure that the system is clean enough for production. Inversely, "normal" CIP does not necessarily ensure that the system is decontaminated. The systems must be decontaminated according to a specified procedure before being taken into use. The procedure can for example include successive rinses with NaOH-solutions, citric acid solutions and pure water. CIP procedures with NaOH-solution and HNO_3-solution can often also be used, but is must be assessed case-by-case. The procedure must be preapproved by the Process Owner or his representative. Systems for dry gasses can be decontaminated by blowing with pure process air or pure nitrogen instead of rinsing with liquids.	
Area of application	

Specifications	Remarks
The requirement applies to process systems. For other systems the requirements are intended as guidance and are in such cases not subject to formal tests. a] Systems must be decontaminated before they are taken into use, according to a specified cleaning procedure. The cleaning procedure must be pre-approved by the customer appointed Project Manager and Project QA	
5.11.15 **Pipe marking**	
Piping must be clearly marked indicating what is carried in the pipes and direction of flow. The marking supports correct operation, maintenance, safety and environmental protection. A standard for pipe marking must be prepared covering the system. Typically, an existing standard for the plant/site is used, but a specific standard for the project/system may be agreed.	
Manual operation At certain points in process systems or process support systems wrong pipe marking may cause production errors (for example addition of the wrong media) or cross-contamination in connections with manual operation or other normal, operation-related actions. These critical locations must be specified in the URS (or another requirement or design document). Pipe marking must at these points be verified by qualification (Q). In all other places, pipe marking must be verified by commissioning (C).	
Area of application The requirement applies to all types of systems. a] Pipe installations must be provided with pipe markings according to the standard in effect on the site.	
5.11.16 **Insulation and cladding**	
Insulation and shielding: Insulation of pipes and tanks as well as other cladding and shielding arrangements are often necessary for safety, energy conservation, etc. Insulation and cladding on systems in classified clean rooms must have a sanitary finish.	
Cold/hot pipes Insulation and cladding of cold pipes and tanks in clean rooms must be sufficient to prevent condensation on the outer surface. Systems that are to be sterilised with pure steam must be sufficiently insulated for the required temperature to be achievable. Verification of insulation which is critical in consideration of sterilisation is done during OQ/PQ via identification and check of the coldest points.	
Insulation specifications Insulation/cladding for all systems is selected and dimensioned as part of the detailed design (if a local standard does not exist already) and must be specified in an insulation specification or similar document.	

Specifications	Remarks
Sanitary execution Assessment of what can be viewed as sanitary finish must be based on international, accepted standards for sanitary design, for example EHEDG Guidelines, 3-A Sanitary Standards or ASME's Bioprocessing Equipment [ASME BPE].	
Area of application The requirement applies to all types of systems. However, the requirement for sanitary finish only applies to those parts of the systems that are installed in clean rooms (room classes A, B and C). a] Insulation and cladding of pipe installations and tanks in classified clean rooms must be sanitary with regard to materials and execution/finish. Insulation of piping and tanks must be carried out with the insulation types and dimensions stated in the insulation specification for the system.	
5.12 **Testing requirements**	
5.12.1 FAT	
System shall be inspected and tested (FAT) at the Vendor's site in the presence of user's representative before delivery.	
Client must be given thirty (30) working days notice in advance of the testing date. The Vendor must ensure that the equipment to be tested conforms to the design requirements prior to notifying Client.	
FAT shall constitute part of the equipment qualification (Installation and Operational Qualification). They will be conducted at the premises of the Vendor in accordance with written procedures and protocols. The Vendor shall write these procedures and submit them to the client for written approval prior to carrying out the tests.	
The Vendor shall be required to undertake the testing and recording of all data in the test documents, witnessed by the client (and/or their representatives or agents).	
The equipment will be checked for its compliance with the specification. Testing shall include, but not be limited to: ➢ Component check ➢ Documentation check ➢ Visual inspection ➢ Verification of drawings ➢ Dimensional check ➢ Functional checks. **Factory Acceptance Test procedures should include:-** ➢ Accuracy/ performance test shall be done on full integrated line instead of Separate single module.(If applicable) ➢ Description of item and function ➢ Checklist to show equipment properly installed, with services connected,	

Specifications	Remarks
equipment clean etc. ➢ Test equipment used and date of calibration	
In the event of the equipment failing to comply with any of the approved test procedures the Vendor shall, at their own expense, make such alterations and modifications to the equipment as are necessary, following an agreed Change Control Procedure. The test procedure(s) shall then be repeated to verify that the equipment meets the Design and Specification. The costs of any such repeat testing, including all expenses incurred by client Inspection Team, shall be borne by the Vendor.	
Only after satisfactory testing may the equipment be packed and dispatched. The approval of the Factory Acceptance Tests shall not constitute acceptance of the equipment.	
5.12.2 SAT	
The Vendor shall be responsible for checking the equipment installation, performing the start-up, and commissioning the equipment to agreed Site Acceptance Procedures. The Vendor shall write these procedures and submit them to Client for approval prior to carrying out the tests.	
Testing shall include inspection of the installation to check that the equipment has been installed correctly and is the equipment specified. It shall also demonstrate that the equipment will operate as intended throughout all anticipated operating ranges. If applicable the testing will include a repeat of the containment level tests as required during the FAT.	
It will be the Vendor's responsibility to ensure that the equipment conforms to the test procedures, and if a failure occurs, to make such modifications as may be necessary, and to re-test the equipment to prove that the equipment meets the requirements. Any modifications shall be subject to an agreed Change Control Procedure. All expenses of such re-testing shall be borne by the Vendor.	
➢ Site Acceptance Test Procedures should include:- ➢ Description of item and its function ➢ Reference to manuals, guidelines, etc., required to carry out a test ➢ Test equipment used, and date of calibration ➢ Test objectives, methods, and acceptance criteria ➢ Test results ➢ Conclusions, including a clear statement of whether the item has been successfully qualified, or not.	
6.0 Technical Requirement	
6.1 **Basic Technical Requirement**	
6.1.1 The layout must be taken into account when determining the layouts of the units.	

Specifications		Remarks
6.1.2	A proposal of a possible installation layout should be added to the documentation.	
6.1.3	The manufacturer has to give the clear details on the total weight, capacity and dimension of the equipment.	
6.1.4	The heat given off by the unit must be stated (inside the room and through exhaust).	
6.1.5	The construction of the complete system should be described in the documentation in detail.	
6.2	**Level of Automation**	
6.2.1	The equipment should operate with minimum operator involvement. The equipment control panel must be provided with a Human machine interface based on English language with appropriate number of recipe of process parameters.	
6.2.2	The equipment should control automatically all critical parameters and detect failure mode automatically. Critical process parameters and failure modes are listed in the respective URS's.	
6.2.3	Human machine interface must be used to enter the process details, which should appear in the print out. Print out must provide results of all critical process parameters and failure alarms.	
7.0	**Transport, Packaging and storage**	
7.1	Delivery to site in presence of the Vendor's representative. Vendor's representative to ensure proper unloading and safe placement of the equipment with client's consent at site.	
7.2	Packaging and shipping of the equipment must take place only after written approval of the FAT. Release is given after inspection in the factory proving unobjectionable condition of the system.	
7.3	The vendor is responsible for installation. Installation to be coordinated with the client's commissioning supervisor.	
7.4	The freight and placement of equipment at site should be under the vendor's representative supervision. In this aspect, Vendor to depute an engineer who will be at site to oversee the unloading, placement of the equipment in the safe area within the client's place.	
7.5	Making necessary transport and lifting equipment available on site will be in equipment vendor scope.	
7.6	Protection against tilting and sliding must be provided.	
7.7	Transport packaging/identification Identification of transport packaging in clear lettering (indelible and water proof), font height min. 100 mm with following contents:	

Specifications	Remarks
• Manufacturer/vendor of system • Contact person principal • Contact person vendor	
7.8 The installation date agreed in the contract must be strictly followed.	

8.0 Good Engineering Practices Requirements

8.1 Equipment must be fabricated following all Good Engineering Practices. The vendor's Quality System must follow applicable national or international standards, such as ISO 9000. Internal quality procedures shall be available for the User's review.	
8.2 The Vendor shall provide a Quality and Project Plan as part of their proposal.	
8.3 The Vendor shall provide a Project Manager/Responsible person for the project to provide a single communication point with the User.	
8.4 Vendor must generate all applicable documents during all phases of equipment fabrication i.e. design, fabrication, testing and shipment as per applicable standards e.g. GAMP.	
8.5 All sensors, controllers, PLC, transmitters, indicators and any other controller or indicators to read, print or control any of the parameter, will have to be calibrated, traceable to national or international standard. Original calibration certificate along with traceability to be submitted by vendor in their IQ file.	
8.6 All material of construction should have test certificates.	
8.7 Vendor must generate and provide all specifications and test certificates of software used in the equipment control and/or monitoring system.	

9.0 Abbreviation

Terms	Abbrevation
AISI	American Iron and Steel Institute (US standardisation authority)
ASME	American Society of Mechanical Engineers (US standardisation authority)
CFR	Code of Federal Regulation (US)
CIP	Cleaning In Place
CR	Change Request
EDR	Enhanced Design Review
DN	Nominal Diameter
EHEDG	European Hygienic Engineering & Design Group
EN	European Norm

Specifications	Remarks

FDA	Food and Drug Administration (US)
GMP / cGMP	Good Manufacturing Practice / current GMP
HVAC	Heating, Ventilation and Air Conditioning
IRS	Installation Requirement Specification
ISPE	International Society for Pharmaceutical Engineering
P&ID	Piping and Instrumentation Diagram
UNS	Unified Numbering System (metallurgy)
URS	User Requirement Specification
USP	United States Pharmacopoeia
WPS	Welding Procedure Specification

10.0 Definitions

Term	Definition
C-marked requirements	Requirements that by requirement classification are assessed to be verified and documented by “Commissioning”.
Media	Used here as a practical term for all materials/substances that are handled in the systems, i.e. materials / substances having direct or indirect contact with the product. It is typically liquids, but can also be gasses and solid substances.
Process Support Systems	Systems which directly support the process operations. These systems do not have contact with product or media in "process systems", but affect process operations, (such as heating, cooling or vacuum) or they deal with a side effect of the process, such as an air emission or a liquid waste [ISPE BPC].
Tag	A unique, unambiguous number identifying a technical installation location for instruments and equipment/components. The installation location is physically marked with the tag. Note: instruments typically also have an ”ID No”, which is independent of installation location (i.e. Tag ≠ ID No). ID No is used to ensure a traceable calibration.
Technical Discipline Specialist	A person from external company who has the necessary, documented skills, qualifications and/or experience to be able to make sound engineering and scientific assessments within the relevant technical area.
Utility systems	Systems that do not have contact with the product or media in "process systems". They are generally site- or building-wide systems that are not tailored to a specific process. For example plant steam and potable water [ISPE BPC].

11.0 References

Ref.	Title
1.	ASME – Bio-processing Equipment – 2004 (or later version) [ASME BPE]

Specifications		Remarks
2.	AWS D18.2 Guide to Weld Discoloration Levels on the Inside of Austenitic	
3.	Stainless Steel Tube (American Welding Society) [AWS]	
4.	Force Institute, Reference colour charts Report 94.34, chart 1 or 2 level C [Force]	
5.	FDA – Guide to inspection of high purity water systems, July 1993 [FDA Water]	
6.	ISPE Baseline Guide: Vol. 5, Commissioning and Qualification [ISPE C&Q]	
7.	ICH Q7 Good Manufacturing Practice for Active Pharmaceutical Ingredients[ICH Q7]	
8.	ISPE Baseline Guide: Vol. 1, Bulk Pharmaceutical Chemicals [ISPE BPC]	
9.	FDA – Code of Federal Regulations, Title 21 [FDA 21 CFR]	
10.	EU Directives 2001/83/EC and 2001/82/EC	

Revision index

Revision	Date	Reason for revision
00	03-02-2014	First draft
01	13-02-2014	Updated as per comments given by HBL on 13-02-2014 by email