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STERILITY ASSURANCE · AUDIT TOOLS

EU GMP Annex 1 (2022)

Exhaustive Audit Questionnaire

Manufacture of Sterile Medicinal Products · EudraLex Volume 4 · C(2022) 5938 final

A line-by-line self-inspection / audit questionnaire covering every requirement section of EU GMP Annex 1 (2022). Each item states the audit question, the expected outcome with its paragraph reference, a compliance status box, and space to record observations and evidence. Paragraph references are a guide — always verify against the current published text.

Site / facility		**Audit reference no.**	
Area / line audited		**Audit type**	
Auditor(s)		**Date**	
Auditee / SME		**Page ___ of ___**	

Status key

C = Compliant **NC** = Non-compliant **OBS** = Observation **N/A** = Not applicable

Tick C or NC in the Status column; for an Observation or N/A, note it in the evidence column.

Coverage

Total: 304 audit items across 10 sections.

Section 1 — Scope

Status key: C = Compliant · NC = Non-compliant · OBS = Observation (note in evidence column) · N/A = Not applicable. *Mark the box and record supporting evidence, gaps or CAPA reference alongside.*

#	Ref	Audit question / expected outcome	Status	Observation & evidence
1.1	§1	**Are facilities, equipment, systems and procedures for all sterile products designed and controlled by applying Quality Risk Management (QRM)?** **Expected outcome:** Design and control apply QRM to prevent microbial, particulate and endotoxin/pyrogen contamination in the final product; any specified limits, frequencies or ranges are treated as minimum requirements.	☐ C ☐ NC ☐ OBS ☐ N/A	
1.2	§1	**Where Annex 1 principles are applied to non-sterile products, is this documented and demonstrated?** **Expected outcome:** The manufacturer clearly documents which principles are applied and demonstrates compliance with those principles.	☐ C ☐ NC ☐ OBS ☐ N/A	

Section 2 — Principle

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#	Ref	Audit question / expected outcome	Status	Observation & evidence
2.1	§2.1(i)	**Are facility, equipment and process appropriately designed, qualified/validated and subject to ongoing verification?** **Expected outcome:** Appropriate technologies (RABS, isolators, robotics, rapid/alternative methods, continuous monitoring) are considered to protect product and aid rapid detection of contaminants.	☐ C ☐ NC ☐ OBS ☐ N/A	
2.2	§2.1(ii)	**Do personnel have adequate qualifications, experience, training and behaviour?** **Expected outcome:** Focus is on the principles of protecting sterile product during manufacturing, packaging and distribution.	☐ C ☐ NC ☐ OBS ☐ N/A	
2.3	§2.1(iii)	**Are processes and monitoring systems designed, commissioned, qualified, monitored and reviewed by suitably knowledgeable personnel?** **Expected outcome:** Personnel have appropriate process, engineering and microbiological knowledge.	☐ C ☐ NC ☐ OBS ☐ N/A	
2.4	§2.1(iv)	**Are raw materials and packaging materials adequately controlled and tested?** **Expected outcome:** Bioburden and endotoxin/pyrogen levels are confirmed suitable for use.	☐ C ☐ NC ☐ OBS ☐ N/A	
2.5	§2.2	**Are processes, equipment, facilities and activities managed per QRM with a design-first priority?** **Expected outcome:** Priority is facility/equipment/process design, then procedures, then monitoring; alternatives are justified by rationale, risk assessment and mitigation; monitoring/testing alone does not assure sterility.	☐ C ☐ NC ☐ OBS ☐ N/A	
2.6	§2.3	**Is a Contamination Control Strategy (CCS) implemented across the facility?** **Expected outcome:** CCS defines all critical control points, assesses effectiveness of all controls and monitoring, is actively reviewed/updated, drives continual improvement and its effectiveness forms part of periodic management review.	☐ C ☐ NC ☐ OBS ☐ N/A	
2.7	§2.4	**Is the collective effectiveness of interrelated contamination-control measures considered together?** **Expected outcome:** Measures are assessed/controlled/monitored individually but their combined effectiveness is evaluated together.	☐ C ☐ NC ☐ OBS ☐ N/A	
2.8	§2.5	**Does the CCS consider all required elements?** **Expected outcome:** CCS addresses plant/process design & documentation, premises & equipment, personnel, utilities, raw material controls, containers/closures, vendor approval, outsourced activities, process risk management, process & sterilisation validation, preventive maintenance, cleaning/disinfection, monitoring systems, prevention mechanisms (trend/RCA/CAPA) and continuous improvement.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
2.9	§2.6	**Is the CCS subject to ongoing and periodic review with change impact assessment?** **Expected outcome:** All aspects reviewed with updates in the PQS; changes assessed for impact on the CCS before and after implementation.	☐ C ☐ NC ☐ OBS ☐ N/A	
2.10	§2.7	**Is sterility assured without sole reliance on any terminal process or finished-product test?** **Expected outcome:** The manufacturer takes all steps/precautions to assure sterility; no sole reliance is placed on a terminal process or finished-product test.	☐ C ☐ NC ☐ OBS ☐ N/A	

Section 3 — Pharmaceutical Quality System (PQS)

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#	Ref	Audit question / expected outcome	Status	Observation & evidence
3.1	§3.1(i)	**Is an effective risk management system integrated into all areas of the product life cycle?** **Expected outcome:** Aim is to minimize microbial contamination and ensure quality of sterile products.	☐ C ☐ NC ☐ OBS ☐ N/A	
3.2	§3.1(ii)	**Does the manufacturer have sufficient knowledge and expertise?** **Expected outcome:** Knowledge covers products, equipment, engineering and manufacturing methods that impact product quality.	☐ C ☐ NC ☐ OBS ☐ N/A	
3.3	§3.1(iii)	**Is root cause analysis of procedural/process/equipment failure performed effectively?** **Expected outcome:** Risk to product is correctly identified so that suitable CAPA is implemented.	☐ C ☐ NC ☐ OBS ☐ N/A	
3.4	§3.1(iv)	**Is risk management applied to the development and maintenance of the CCS?** **Expected outcome:** Contamination risks are identified, assessed, reduced/eliminated and controlled, with documented rationale including residual risk acceptance.	☐ C ☐ NC ☐ OBS ☐ N/A	
3.5	§3.1(v)	**Does senior management effectively oversee the state of control?** **Expected outcome:** Risk management outcomes are reviewed regularly, on change, on emerging problems and during periodic product quality review.	☐ C ☐ NC ☐ OBS ☐ N/A	
3.6	§3.1(vi)	**Do finishing, storage and transport processes protect the sterile product?** **Expected outcome:** Container integrity, contamination risk and avoidance of degradation are addressed, with products stored per registered conditions.	☐ C ☐ NC ☐ OBS ☐ N/A	
3.7	§3.1(vii)	**Do persons certifying/releasing product have appropriate access, knowledge and experience?** **Expected outcome:** They can determine whether product was made per registered specifications/approved process and is of required quality.	☐ C ☐ NC ☐ OBS ☐ N/A	
3.8	§3.2	**Are non-conformities investigated before certification/release?** **Expected outcome:** Sterility failures, EM excursions and deviations are investigated for process/product impact and other affected batches; scope inclusion/exclusion is justified and recorded.	☐ C ☐ NC ☐ OBS ☐ N/A	

Section 4 — Premises

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#	Ref	Audit question / expected outcome	Status	Observation & evidence
4.1	§4.1	**Is manufacture carried out in appropriate cleanrooms entered via airlocked change rooms?** **Expected outcome:** Cleanrooms/change rooms are maintained to appropriate cleanliness, supplied with appropriately filtered air, with scientifically justified controls and monitoring.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.2	§4.2	**Are component prep, product prep and filling separated appropriately?** **Expected outcome:** Technical and operational separation within the cleanroom/facility prevents mix-up and contamination.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.3	§4.3	**Are RABS or isolators considered in the CCS?** **Expected outcome:** Their use is considered to minimize contamination from human intervention; alternatives are justified.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.4	§4.4	**Are the four cleanroom grades (A–D) correctly defined and applied?** **Expected outcome:** Grade A critical zone under localised UDAF within RABS/isolators (qualified across the whole grade A area); grade B background; grade C/D for less critical/terminal operations.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.5	§4.5	**Are all exposed surfaces smooth, impervious and unbroken?** **Expected outcome:** Surfaces minimize shedding/accumulation of particles or micro-organisms.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.6	§4.6	**Are recesses minimized to facilitate cleaning?** **Expected outcome:** Projecting ledges/shelves/cupboards/equipment minimized; doors avoid recesses; sliding doors generally avoided.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.7	§4.7	**Are cleanroom materials selected to minimize particles and permit repeated disinfection?** **Expected outcome:** Materials permit repeated application of cleaning, disinfectant and sporicidal agents.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.8	§4.8	**Are ceilings designed and sealed against contamination from the space above?** **Expected outcome:** Ceilings prevent contamination from the void above.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.9	§4.9	**Are sinks and drains prohibited in grade A/B and controlled elsewhere?** **Expected outcome:** No sinks/drains in grade A/B; air breaks fitted elsewhere; floor drains have traps/water seals, regularly cleaned/disinfected/maintained.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.10	§4.10	**Is transfer of equipment/materials assessed as a major contamination source?** **Expected outcome:** Activities that could compromise cleanliness are assessed and, if not eliminable, appropriate controls applied.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
4.11	§4.11	**Is transfer into and out of grade A/B unidirectional and validated?** **Expected outcome:** Items sterilised via double-ended sterilisers where possible; validated alternative transfer processes otherwise; removal via a separate unidirectional process.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.12	§4.12	**Are airlocks designed to separate areas and minimize contamination?** **Expected outcome:** Personnel/material airlocks separated where possible; flushed with filtered air; final stage at same grade at rest; separate change rooms for entering/leaving grade B desirable.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.13	§4.13	**Are airlock/pass-through doors interlocked or alarmed appropriately?** **Expected outcome:** Entry/exit doors not opened simultaneously; interlock for grade A/B; visual/audible warning for grade C/D; time delay where required.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.14	§4.14	**Is a filtered air supply maintaining positive pressure/airflow provided?** **Expected outcome:** ≥10 Pa (guidance) between adjacent grades; critical zone protected; containment modifications applied where needed; air into a critical zone sourced from same/higher grade.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.15	§4.15	**Are airflow visualisation studies performed and retained?** **Expected outcome:** Performed at rest and in operation, demonstrating no lower-to-higher grade ingress; documented; video recordings retained; feed into the EM programme.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.16	§4.16	**Are air pressure difference indicators fitted and critical differentials monitored?** **Expected outcome:** Critical differentials continuously monitored/recorded with a warning system; alarm overrides controlled; alarm delays justified in CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.17	§4.17	**Do facilities permit observation of production from outside grade A/B?** **Expected outcome:** Windows or remote cameras give a full view for observation/supervision without entry.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.18	§4.18	**Are isolators/RABS designed to separate grade A from the surrounding room?** **Expected outcome:** Entry/removal hazards minimized and supported by high-capability transfer technologies or validated systems.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.19	§4.19	**Does the barrier design ensure appropriate critical-zone conditions?** **Expected outcome:** Open isolators: grade A with first air and UDAF; closed isolators: grade A with adequate protection; negative-pressure only where containment essential; RABS: grade A UDAF with first air and positive airflow.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.20	§4.20	**Is the background environment for isolators/RABS appropriate and justified?** **Expected outcome:** Open isolator ≥ grade C, closed isolator ≥ grade D, RABS (aseptic) ≥ grade B; based on risk assessment justified in CCS; airflow studies at open isolator interfaces.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
4.21	§4.21	**Are glove systems and their integrity testing controlled?** **Expected outcome:** Gloves demonstrate mechanical/chemical resistance; replacement frequency in CCS; isolator glove integrity tested at least at start/end of each batch or campaign plus visual checks; RABS gloves sterilised/bio-decontaminated before campaigns.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.22	§4.22	**Are decontamination methods for RABS/isolators defined and controlled?** **Expected outcome:** Cleaning precedes bio-decontamination; agents show no adverse product impact; isolator bio-decontamination automated/validated with sporicidal agent rendering interior free of viable organisms; RABS routine sporicidal disinfection validated.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.23	§4.23	**Are cleanrooms and clean air equipment qualified to required characteristics?** **Expected outcome:** Qualified per required environment; appropriate cleanliness in 'at rest' and 'operational' states.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.24	§4.24	**Is qualification performed per Annex 15 and differentiated from EM?** **Expected outcome:** Cleanroom qualification (incl. classification) is clearly differentiated from operational environmental monitoring.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.25	§4.25	**Does qualification include the full set of relevant tests?** **Expected outcome:** Filter leakage/integrity, airflow volume/velocity, air pressure difference, airflow direction/visualisation, microbial airborne/surface, temperature, humidity, recovery and containment leak (per ISO 14644).	☐ C ☐ NC ☐ OBS ☐ N/A	
4.26	§4.26	**Is cleanroom classification scheduled and performed correctly?** **Expected outcome:** Classification measures total particle concentration; scheduled to avoid impact on process/product; initial during simulated operations; reclassification during simulated operations or APS.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.27	§4.27	**Are total particles ≥0.5 and ≥5 µm measured against Table 1?** **Expected outcome:** Measured at rest and in simulated operations within Table 1 limits.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.28	§4.28	**Are sampling locations per ISO 14644-1 with additional critical points?** **Expected outcome:** Minimum locations per ISO 14644-1; additional grade A/B locations; all critical processing points (e.g. point of fill, feeder bowls) evaluated by documented risk assessment.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.29	§4.29	**Are 'at rest' and 'in operation' states and clean-up period defined?** **Expected outcome:** Classification in both states; 'at rest' achieved after a clean-up period (guidance <20 min) determined at qualification and adhered to.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.30	§4.30	**Is UDAF air speed justified and within guidance?** **Expected outcome:** 0.36–0.54 m/s (guidance) homogeneous at the working position unless justified in CCS; correlated with airflow visualisation.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
4.31	§4.31	**Is microbial contamination level determined during qualification (Table 2)?** **Expected outcome:** Sampling locations by documented risk assessment; Table 2 limits met; both 'at rest' and 'in operation'.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.32	§4.32	**Is requalification periodic and complete within maximum intervals?** **Expected outcome:** Includes classification, final-filter integrity, airflow volume, pressure differentials and air velocity/recovery; grade A & B ≤6 months, grade C & D ≤12 months; also after remedial action or significant change.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.33	§4.33	**Is disinfection performed per a validated written programme?** **Expected outcome:** Prior cleaning removes surface contamination; more than one disinfectant type; periodic sporicidal agent; monitoring of effectiveness and flora changes.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.34	§4.34	**Is the disinfection process validated?** **Expected outcome:** Validation demonstrates suitability/effectiveness for the manner/surface of use and supports in-use expiry of prepared solutions.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.35	§4.35	**Are grade A/B disinfectants sterile and controlled?** **Expected outcome:** Grade A/B disinfectants/detergents sterile (grade C/D where CCS requires); in-house dilutions prepared to prevent contamination, monitored, and stored only for a defined period.	☐ C ☐ NC ☐ OBS ☐ N/A	
4.36	§4.36	**Where fumigation/vapour disinfection (e.g. VHP) is used, is it validated?** **Expected outcome:** Effectiveness of agent and dispersion system understood and validated.	☐ C ☐ NC ☐ OBS ☐ N/A	

Section 5 — Equipment

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#	Ref	Audit question / expected outcome	Status	Observation & evidence
5.1	§5.1	**Is a written, detailed equipment design description available and current?** **Expected outcome:** Includes P&IDs as appropriate; forms part of the initial qualification package and is kept up to date.	☐ C ☐ NC ☐ OBS ☐ N/A	
5.2	§5.2	**Are equipment monitoring requirements defined in URS and alarms managed?** **Expected outcome:** Requirements defined in URS and confirmed at qualification; alarm events acknowledged and evaluated for trends; critical alarms reviewed immediately.	☐ C ☐ NC ☐ OBS ☐ N/A	
5.3	§5.3	**Is equipment designed for maintenance outside the cleanroom where practicable?** **Expected outcome:** Where in-cleanroom maintenance occurs, precautions (access restriction, protocols, additional cleaning/disinfection/EM) are considered; sterilisation performed after full reassembly where possible.	☐ C ☐ NC ☐ OBS ☐ N/A	
5.4	§5.4	**Is the cleaning process validated?** **Expected outcome:** Validated to remove residue/debris impairing disinfection and to minimize chemical, microbial and particulate contamination prior to disinfection.	☐ C ☐ NC ☐ OBS ☐ N/A	
5.5	§5.5	**Are direct and indirect product-contact parts sterilised for aseptic processes?** **Expected outcome:** Both direct (e.g. filling needles/pumps) and indirect critical parts (e.g. stopper bowls, guides) are sterilised.	☐ C ☐ NC ☐ OBS ☐ N/A	
5.6	§5.6	**Are key systems qualified, monitored and maintained with approved return to use?** **Expected outcome:** Sterilisers, air handling/filtration and water systems are qualified, monitored and on planned maintenance; return to use is approved.	☐ C ☐ NC ☐ OBS ☐ N/A	
5.7	§5.7	**Is unplanned maintenance impact on sterility assessed and recorded?** **Expected outcome:** Where unplanned maintenance affects sterility-critical equipment, impact on product sterility is assessed and recorded.	☐ C ☐ NC ☐ OBS ☐ N/A	
5.8	§5.8	**Is conveyor transfer between grades controlled?** **Expected outcome:** A conveyor belt does not pass a partition between grade A/B and a lower-cleanliness area unless continually sterilised (e.g. sterilising tunnel).	☐ C ☐ NC ☐ OBS ☐ N/A	
5.9	§5.9	**Are particle counters and sampling systems qualified?** **Expected outcome:** Counters/tubing qualified; tube typically ≤1 m with minimized bends; portable counters for classification; isokinetic heads used and correctly oriented in UDAF.	☐ C ☐ NC ☐ OBS ☐ N/A	

Section 6 — Utilities

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#	Ref	Audit question / expected outcome	Status	Observation & evidence
6.1	§6.1	**Are utility controls commensurate with risk and documented in the CCS?** **Expected outcome:** Nature/extent of controls determined by risk assessment and documented in the CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.2	§6.2	**Are higher-risk utilities identified?** **Expected outcome:** Utilities that directly contact product, contact materials that become product, contact product-contact surfaces, or otherwise directly impact product are identified as higher risk.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.3	§6.3	**Are utilities designed, installed, qualified, operated, maintained and monitored?** **Expected outcome:** The utility system functions as expected across its lifecycle.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.4	§6.4	**Are high-risk utility critical parameters/CQAs trend analysed?** **Expected outcome:** Results subject to regular trend analysis to confirm continued system capability.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.5	§6.5	**Are utility installation records maintained throughout the lifecycle?** **Expected outcome:** Current drawings/schematics, construction materials, specifications, pipeline details, tanks/vessels, valves/filters/drains/sampling/user points.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.6	§6.6	**Are pipes/ducts kept out of cleanrooms where possible?** **Expected outcome:** Where unavoidable, installed without recesses/unsealed openings/difficult surfaces, allowing cleaning/disinfection of outer surfaces.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.7	§6.7	**Is the water treatment/distribution system designed to prevent contamination?** **Expected outcome:** Designed/qualified/monitored to prevent microbial contamination and minimize particulate/endotoxin (e.g. sloped piping, no dead legs); filters monitored; water meets the relevant Pharmacopeia monograph.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.8	§6.8	**Are water systems qualified/validated including seasonal variation?** **Expected outcome:** Maintain appropriate physical, chemical and microbial control accounting for seasonal variation.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.9	§6.9	**Is turbulent flow maintained and flow rate monitored?** **Expected outcome:** Water flow remains turbulent to minimize biofilm; flow rate established at qualification and routinely monitored.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.10	§6.10	**Is WFI produced, stored and distributed appropriately?** **Expected outcome:** Produced by distillation or an equivalent process; stored/distributed to minimize microbial growth (e.g. constant circulation >70°C).	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
6.11	§6.11	**Are WFI tank vent filters controlled?** **Expected outcome:** Hydrophobic vent filters not a contamination source; integrity tested before installation and after use; condensation prevented (e.g. heating).	☐ C ☐ NC ☐ OBS ☐ N/A	
6.12	§6.12	**Is water system sanitisation scheduled and verified before release?** **Expected outcome:** Sterilisation/disinfection/regeneration on a schedule and as remedial action; chemical disinfection followed by validated rinsing; testing after; results approved before returning to use/release.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.13	§6.13	**Is ongoing chemical/microbial water monitoring performed?** **Expected outcome:** Regular monitoring against compendial expectations; alert levels from qualification, periodically reassessed; sampling all outlets/points of use with ≥1 representative daily sample of manufacturing water.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.14	§6.14	**Are water alert/action limit excursions investigated?** **Expected outcome:** Alert excursions documented/reviewed/investigated (isolated vs trend); action limit excursions root-caused with product/process impact assessed.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.15	§6.15	**Does the WFI system include continuous monitoring?** **Expected outcome:** Continuous monitoring such as TOC and conductivity, with risk-based sensor locations.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.16	§6.16	**Is pure/clean steam generation controlled?** **Expected outcome:** Feed water appropriately purified; generator designed/qualified/operated so steam meets defined chemical and endotoxin levels.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.17	§6.17	**Is steam used as a direct sterilising agent of suitable quality?** **Expected outcome:** No contaminating additives; condensate meets the WFI monograph; representative sampling; non-condensable gases, dryness value and superheat assessed against validated parameters.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.18	§6.18	**Are product-contact gases of appropriate quality?** **Expected outcome:** Appropriate chemical/particulate/microbial quality; all parameters (incl. oil and water content) specified per use, generation design and Pharmacopeia/product requirements.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.19	§6.19	**Are gases in aseptic processes filtered and controlled?** **Expected outcome:** Filtered through a sterilising grade filter (max 0.22 µm) at point of use; batch/vent filters integrity tested and reviewed at release; post-filter pipework sterilised; periodic microbial monitoring at point of use.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.20	§6.20	**Is backflow from vacuum/pressure systems prevented?** **Expected outcome:** Mechanism(s) prevent backflow when the vacuum/pressure system is shut off where backflow poses a risk.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
6.21	§6.21	**Are hydraulic/heating/cooling major items located outside the filling room?** **Expected outcome:** Located outside where possible, with controls to contain spillage and cross-contamination from system fluids.	☐ C ☐ NC ☐ OBS ☐ N/A	
6.22	§6.22	**Are leaks from these systems detectable?** **Expected outcome:** Leaks presenting product risk are detectable (e.g. a leakage indication system).	☐ C ☐ NC ☐ OBS ☐ N/A	

Section 7 — Personnel

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#	Ref	Audit question / expected outcome	Status	Observation & evidence
7.1	§7.1	**Are there sufficient, suitably qualified and experienced personnel?** **Expected outcome:** Sufficient trained/experienced personnel for the manufacture and testing of sterile products and the specific technologies used.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.2	§7.2	**Is the number of personnel in cleanrooms minimized and a maximum set?** **Expected outcome:** Only the minimum required present; a documented maximum determined and considered during qualification and APS so as not to compromise sterility assurance.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.3	§7.3	**Do all cleanroom-access personnel receive regular training and assessment?** **Expected outcome:** Regular training, gowning qualification and assessment covering microbiology/hygiene basics, cleanroom practices, contamination control, aseptic technique and patient safety implications; level based on criticality.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.4	§7.4	**Is aseptic gowning qualification confirmed and periodically reassessed?** **Expected outcome:** Grade A/B personnel trained in aseptic gowning/behaviour; confirmed by visual and microbial assessment at least annually; unsupervised access restricted to qualified staff who passed gowning and a successful APS.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.5	§7.5	**Is entry of unqualified personnel to grade A/B controlled?** **Expected outcome:** Unqualified personnel do not enter grade B or grade A in operation except via written exceptional procedures, with supervision by an authorised person, impact assessment and recording per PQS.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.6	§7.6	**Is there a disqualification and requalification system?** **Expected outcome:** Disqualification based on adverse monitoring trends or a failed APS; retraining/requalification (incl. APS participation where relevant) before returning to aseptic work.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.7	§7.7	**Are hygiene standards and health reporting enforced?** **Expected outcome:** High personal hygiene; personnel report health conditions increasing shedding; competent-person guidance and procedures for undue microbial hazards.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.8	§7.8	**Are personnel handling tissue/cultures controlled?** **Expected outcome:** Those handling human/animal tissue or other cultures do not enter clean areas unless defined, effective decontamination/entry procedures are followed and documented.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.9	§7.9	**Are prohibited personal items excluded from clean areas?** **Expected outcome:** No wristwatches, make-up, jewellery, mobile phones or non-essential items; manufacturer-supplied, cleanable cleanroom electronics are a controlled exception in the CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
7.10	§7.10	**Is gowning and hand washing performed per written procedure?** **Expected outcome:** Designed to minimize contamination of cleanroom clothing and transfer of contaminants.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.11	§7.11	**Is clothing appropriate, checked and qualified?** **Expected outcome:** Clothing appropriate to process/grade; visually checked before/after gowning and on exit; sterilised garments within hold time with integral packaging; reusable garments replaced if damaged or at a qualified frequency; garment qualification includes testing.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.12	§7.12	**Is clothing chosen to limit shedding?** **Expected outcome:** Clothing limits shedding due to operator movement.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.13	§7.13	**Is grade-specific clothing worn as described?** **Expected outcome:** Grade B (incl. grade A interventions) fully sterilised gowning (headgear, mask, goggles, over-boots, double sterile gloves); grade C and D as specified; additional gowning in C/D per CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.14	§7.14	**Is gowning performed in appropriately graded change rooms?** **Expected outcome:** No outdoor clothing/socks into change rooms leading to grade B/C; facility suits/socks worn before entry; suits/socks not a contamination risk.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.15	§7.15	**Does each grade B/A entry use fresh sterilised garments?** **Expected outcome:** Every operator gowns into clean, sterilised garments (incl. eye coverings, masks) at each entry; maximum wear period defined in garment qualification.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.16	§7.16	**Are gloves disinfected and damaged garments changed immediately?** **Expected outcome:** Gloves regularly disinfected during operations; garments/gloves changed immediately if damaged and presenting contamination risk.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.17	§7.17	**Is reusable cleanroom clothing laundered under a qualified process?** **Expected outcome:** Laundered in a segregated facility using a qualified process preventing damage/contamination; inspected after washing; maximum laundry/sterilisation cycles defined.	☐ C ☐ NC ☐ OBS ☐ N/A	
7.18	§7.18	**Are non-critical activities and movements minimized?** **Expected outcome:** Non-critical activities minimized; movement slow/controlled/methodical; aseptic technique maintained; movement adjacent to the critical zone restricted; first air not obstructed; airflow visualisation reviewed in training.	☐ C ☐ NC ☐ OBS ☐ N/A	

Section 8 — Production and Specific Technologies

Status key: C = Compliant · NC = Non-compliant · OBS = Observation (note in evidence column) · N/A = Not applicable. *Mark the box and record supporting evidence, gaps or CAPA reference alongside.*

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.1	§8.1	**Is component/material preparation for terminally sterilised products in the correct grade?** **Expected outcome:** At least grade D (at least grade C for high/unusual microbial risk; ointments/creams/suspensions/emulsions at least grade C before terminal sterilisation).	☐ C ☐ NC ☐ OBS ☐ N/A	
8.2	§8.2	**Are primary containers/components cleaned by validated processes?** **Expected outcome:** Particle, endotoxin/pyrogen and bioburden contamination appropriately controlled.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.3	§8.3	**Is filling of products for terminal sterilisation in at least grade C?** **Expected outcome:** Filling carried out in at least a grade C environment.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.4	§8.4	**Is unusual-risk filling performed in grade A with grade C background?** **Expected outcome:** Where the CCS identifies unusual environmental risk (slow filling, wide-necked or exposed containers), product is filled in grade A with at least a grade C background.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.5	§8.5	**Is a bulk filtration step and max prep-to-fill time applied?** **Expected outcome:** A microorganism-retaining filtration step reduces bioburden/particles where possible, with a maximum permissible time between preparation and filling.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.6	§8.6	**Are terminally sterilised operations mapped to grades per Table 3?** **Expected outcome:** Operations assigned to grades A/C/D per Table 3.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.7	§8.7	**Is the aseptic process clearly defined with controlled risks?** **Expected outcome:** Risks identified, assessed and controlled; CCS defines acceptance criteria and monitoring; residual risks formally documented.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.8	§8.8	**Are contamination precautions applied through all aseptic stages?** **Expected outcome:** Precautions per CCS during preparation of the aseptic environment and all stages until final container sealing; particle/fibre-generating materials minimized.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.9	§8.9	**Are RABS/isolators/robotics used to reduce critical interventions?** **Expected outcome:** Considered to reduce the need for critical interventions into grade A and minimize contamination.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.10	§8.10	**Are aseptic operations mapped to grades per Table 4?** **Expected outcome:** Operations assigned to grades A/B/C/D per Table 4.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.11	§8.11	**For non-filterable final formulations, are alternative controls applied?** **Expected outcome:** Product/component contact equipment sterilised; raw materials/intermediates sterilised and aseptically added; bulk solutions/intermediates sterilised.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.12	§8.12	**Is unwrapping/assembly and line set-up/filling performed in grade A/B?** **Expected outcome:** Treated as aseptic processes performed in grade A with a grade B background (isolator background per §4.20).	☐ C ☐ NC ☐ OBS ☐ N/A	
8.13	§8.13	**Is aseptic prep/filling of ointments/creams/suspensions/emulsions in grade A/B?** **Expected outcome:** Performed in grade A with grade B background when exposed and not subsequently filtered or terminally sterilised (isolator/RABS per §4.20).	☐ C ☐ NC ☐ OBS ☐ N/A	
8.14	§8.14	**Are aseptic connections performed and verified appropriately?** **Expected outcome:** In grade A with grade B background unless sterilised in place or made with intrinsic sterile connection devices; effectiveness assessed and verified.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.15	§8.15	**Are aseptic manipulations minimized by engineering design?** **Expected outcome:** Preassembled and sterilised equipment used; product-contact piping pre-assembled and sterilised in place wherever feasible.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.16	§8.16	**Is there an authorised list of qualified interventions?** **Expected outcome:** Allowed inherent and corrective interventions authorised, designed to minimize contamination, evaluated via risk management and APS; non-qualified interventions only exceptionally with QA authorisation, risk-assessed, recorded and investigated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.17	§8.17	**Are interventions and stoppages recorded in the batch record?** **Expected outcome:** Each stoppage/intervention documented with associated time, duration and operators involved.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.18	§8.18	**Are aseptic processing durations minimized and validated?** **Expected outcome:** Defined validated maximum times for holding, sterilised-equipment/component/container use, decontaminated-environment use, prep-to-sterilisation/filtration, sterilised-product holding, aseptic processing and filling times.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.19	§8.19	**Are aseptic operations regularly observed by experts?** **Expected outcome:** Observed on a regular basis by personnel with aseptic-processing expertise to verify correct performance and address inappropriate practices.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.20	§8.20	**Are open primary packaging containers maintained under grade A?** **Expected outcome:** Maintained under grade A with the appropriate background for the technology (§4.20).	☐ C ☐ NC ☐ OBS ☐ N/A	
8.21	§8.21	**Are final containers closed by validated methods?** **Expected outcome:** Closure achieved by appropriately validated methods.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.22	§8.22	**Is container closure integrity of fusion-sealed containers controlled?** **Expected outcome:** Critical seal parameters controlled/monitored; glass ampoules, BFS units and containers ≤100 ml 100% integrity tested; >100 ml reduced sampling only if scientifically justified; visual inspection is not an acceptable integrity test.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.23	§8.23	**Is integrity of non-fusion systems checked by validated methods?** **Expected outcome:** Samples checked using validated methods with a scientifically justified sampling plan based on knowledge/experience and component specifications.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.24	§8.24	**Are vacuum-sealed containers tested for vacuum maintenance?** **Expected outcome:** Tested after a predetermined period prior to release and during shelf life.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.25	§8.25	**Does CCIT validation consider transport/shipping impact?** **Expected outcome:** Considers transportation/shipping (e.g. decompression, extreme temperatures) that may affect integrity.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.26	§8.26	**Is vial-capping particle generation controlled?** **Expected outcome:** Where large non-viable particle quantities may be generated, measures such as a separate station with adequate air extraction are used.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.27	§8.27	**Is vial capping performed under appropriate conditions?** **Expected outcome:** Aseptic (sterilised caps) or clean process; vials protected by grade A conditions/air supply until crimped; background at least grade D; manual capping in grade A isolator or grade A with grade B background.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.28	§8.28	**Are missing/displaced stoppers rejected before clean-process capping?** **Expected outcome:** Vials with missing/displaced stoppers rejected prior to capping; qualified automated stopper-height detection in place.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.29	§8.29	**Are capping-station human interventions controlled?** **Expected outcome:** Appropriate technological/organisational measures prevent direct contact and minimize contamination; RABS/isolators may assist.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.30	§8.30	**Are all filled parenteral containers inspected and defects managed?** **Expected outcome:** 100% individual inspection; defect classification/criticality by risk; batch defect trending; a maintained defect library used for training; critical defects investigated if found later.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.31	§8.31	**Is manual inspection controlled and operators qualified?** **Expected outcome:** Controlled illumination/background; qualified inspection rates; operator visual inspection qualification at least annually using defect-library samples and worst cases; eyesight checks; minimized distractions and appropriate breaks.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.32	§8.32	**Is automated inspection validated and challenged?** **Expected outcome:** Validated to detect known defects at least equal to manual inspection; challenged with representative defects before start-up and at intervals.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.33	§8.33	**Are inspection results recorded and trended?** **Expected outcome:** Results recorded; defect types/numbers and reject levels trended on statistical principles; market impact assessed on adverse trends.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.34	§8.34	**Is terminal sterilisation used where possible?** **Expected outcome:** Finished product terminally sterilised where possible (greater assurance than filtration/aseptic); post-aseptic terminal heat treatment considered where terminal sterilisation is not possible.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.35	§8.35	**Is sterilisation equipment/cycle selection science-based?** **Expected outcome:** Selection, design and location based on scientific principles/data demonstrating repeatability/reliability; parameters defined and, where critical, controlled/monitored/recorded.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.36	§8.36	**Are all sterilisation processes validated?** **Expected outcome:** Validated considering composition, storage and max time to sterilisation; suitability/efficacy demonstrated for all load parts via physical measurements and, where appropriate, BIs.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.37	§8.37	**Is special attention given to non-compendial methods?** **Expected outcome:** Particular attention where the method is not in the current Pharmacopoeia or used for a non-simple aqueous solution; heat sterilisation is the method of choice where possible.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.38	§8.38	**Are validated loading patterns established and revalidated?** **Expected outcome:** Validated load patterns for all processes with periodic revalidation; max and min loads considered.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.39	§8.39	**Is sterilising-process validity reviewed at intervals?** **Expected outcome:** Reviewed/verified at risk-based intervals; heat cycles revalidated at least annually for worst-case load patterns; other loads at a CCS-justified frequency.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.40	§8.40	**Are routine operating parameters established and followed?** **Expected outcome:** Physical parameters and loading patterns established and adhered to for all sterilisation processes.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.41	§8.41	**Are non-conforming sterilisation cycles detected and investigated?** **Expected outcome:** Mechanisms detect cycles not conforming to validated parameters; failed/deviated cycles investigated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.42	§8.42	**Are biological indicators used and controlled appropriately?** **Expected outcome:** BIs at appropriate locations support validation; stored/used per instructions; positive controls each cycle (e.g. EO); precautions prevent contamination transfer; BI results alone do not override critical parameters.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.43	§8.43	**Is BI reliability assured?** **Expected outcome:** Suppliers qualified; transport/storage controlled; population, purity and identity of a new BI batch verified before use; other critical parameters (D-, Z-value) may use the qualified supplier certificate.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.44	§8.44	**Are sterilised and non-sterilised items clearly differentiated?** **Expected outcome:** Clear labelling/electronic tracking indicating sterilised status; indicators (e.g. autoclave tape) show only that the process occurred, not sterility or SAL.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.45	§8.45	**Are sterilisation records available and reviewed at release?** **Expected outcome:** Records for each run with a unique cycle identifier; conformity reviewed/approved as part of batch certification/release.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.46	§8.46	**Are items sterilised by validated methods with post-sterilisation protection?** **Expected outcome:** Validated methods appropriate to material; protection against recontamination; maximum hold time for stored sterilised items; sealed-packaging process performed before sterilisation.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.47	§8.47	**Is transfer of sealed sterilised items into grade A validated?** **Expected outcome:** Via validated methods (airlocks/pass-throughs) with exterior disinfection; RTP technology considered; effectiveness in controlling contamination demonstrated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.48	§8.48	**Is sterile packaging qualified and its sealing validated?** **Expected outcome:** Packaging qualified to minimize contamination and for compatibility with the sterilisation method; sealing process validated; integrity of the sterile barrier checked before use.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.49	§8.49	**Are non-sterilisable necessary items disinfected and transferred by validated processes?** **Expected outcome:** Effective validated disinfection/transfer; protection against recontamination; included in the EM programme.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.50	§8.50	**Is each heat sterilisation cycle recorded with safeguards?** **Expected outcome:** Recorded with suitable accuracy/precision; safeguards/redundancy (e.g. duplex probes to independent control/monitoring) detect and abort/fail non-conforming cycles.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.51	§8.51	**Are temperature probe positions validated?** **Expected outcome:** Control/recording probe positions determined at validation and verified with an independent monitoring probe at the same position.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.52	§8.52	**Does the whole load reach temperature before timing starts?** **Expected outcome:** Sterilising time starts only after the whole load reaches the required temperature; reference-probe load control within a defined range before cycle commencement.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.53	§8.53	**Are cooling-phase contamination precautions in place?** **Expected outcome:** Precautions against contamination during cooling; any cooling liquid/gas contacting product or sterilised material is sterilised.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.54	§8.54	**Where parametric release is authorised, is it robustly controlled?** **Expected outcome:** Robust lifecycle validation and routine monitoring, periodically reviewed (Annex 17).	☐ C ☐ NC ☐ OBS ☐ N/A	
8.55	§8.55	**Is moist heat sterilisation performed by suitable systems?** **Expected outcome:** Steam (direct/indirect) or other systems (e.g. superheated water) suitable for the container type.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.56	§8.56	**Are items dry and packaged for air removal/steam penetration?** **Expected outcome:** Items (other than sealed-container products) dry and in a protective barrier allowing air removal and steam penetration; all loads dry on removal, confirmed by visual inspection.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.57	§8.57	**Are porous (hard goods) cycles monitored and items inspected?** **Expected outcome:** Time, temperature and pressure monitored/recorded; each item inspected for damage/packaging integrity/moisture; unfit items removed and investigated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.58	§8.58	**Is temperature recorded at the chamber drain for prevacuum/SIP?** **Expected outcome:** For prevacuum autoclaves, temperature recorded at the chamber drain throughout; for SIP, at appropriate condensate drain locations.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.59	§8.59	**Are porous and fluid cycle validations complete?** **Expected outcome:** Porous: equilibration/exposure time, pressure-temperature correlation, min/max exposure temperature; fluids: temperature, time and/or F0; CPP with defined limits/tolerances confirmed at validation and routine acceptance.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.60	§8.60	**Are steriliser leak tests performed periodically?** **Expected outcome:** Normally weekly when a vacuum phase is used or the system returns to sub-ambient pressure.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.61	§8.61	**Is adequate air removal assured?** **Expected outcome:** Air removal test cycle (normally daily) or air detector system for autoclaves/lyophiliser chambers; loads designed for effective air removal and free draining.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.62	§8.62	**Is distortion of non-rigid containers prevented?** **Expected outcome:** BFS/FFS containers protected by appropriate cycle design/control (pressure, heating/cooling rates, loading).	☐ C ☐ NC ☐ OBS ☐ N/A	
8.63	§8.63	**Are steam-in-place systems designed, validated and monitored?** **Expected outcome:** All parts subjected to required treatment; monitored for temperature/pressure/time at representative slowest-to-heat locations; system remains integral post-SIP (positive pressure or sterilising vent filter).	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.64	§8.64	**In superheated-water fluid cycles, does water reach all contact points?** **Expected outcome:** Heated water consistently reaches all required contact points; initial temperature mapping; routine nozzle/drain checks.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.65	§8.65	**Is superheated-water fluid load validation complete?** **Expected outcome:** Temperature mapping of the entire load, heat penetration and reproducibility studies; routine probes correlated to worst-case positions.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.66	§8.66	**Is dry heat sterilisation/depyrogenation controlled?** **Expected outcome:** Time/temperature produce adequate reproducible lethality and/or endotoxin inactivation within established limits, in an oven or continuous tunnel.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.67	§8.67	**Are dry heat tunnels configured and validated?** **Expected outcome:** Airflow protects the grade A sterilising zone via pressure differentials; HEPA-filtered air with periodic (at least biannual) filter integrity tests; CPP incl. belt speed/dwell, temperatures, heat penetration/distribution and airflow profiles.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.68	§8.68	**Does thermal depyrogenation achieve required endotoxin reduction?** **Expected outcome:** Validated to provide a suitable Fh value and a minimum 3 log10 endotoxin reduction; no additional sterilisation demonstration then required.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.69	§8.69	**Are endotoxin-spiked containers used in depyrogenation validation?** **Expected outcome:** Representative containers spiked and fully reconciled; endotoxin quantification and recovery efficiency demonstrated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.70	§8.70	**Are dry heat ovens controlled and validated?** **Expected outcome:** Positive pressure relative to lower grades; HEPA-filtered air; CPP incl. temperature, exposure time, chamber pressure, air speed, air quality, heat penetration/distribution and load pattern (min/max loads).	☐ C ☐ NC ☐ OBS ☐ N/A	
8.71	§8.71	**Is radiation sterilisation used and controlled appropriately?** **Expected outcome:** Used mainly for heat-sensitive materials; UV irradiation is not acceptable; ionising radiation per Annex 12.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.72	§8.72	**Does radiation validation consider density variation?** **Expected outcome:** Effects of variation in product/package density considered.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.73	§8.73	**Is ethylene oxide used only when unavoidable and degassing validated?** **Expected outcome:** Used only when no other method is practicable; validation shows no damaging product effect and residual EO/reaction products reduced to defined limits.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.74	§8.74	**Is direct gas-cell contact ensured for EO?** **Expected outcome:** Precautions avoid organisms enclosed in crystals/dried protein; packaging nature/porosity/quantity controlled.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.75	§8.75	**Is load conditioning before EO exposure controlled?** **Expected outcome:** Materials brought to required humidity/temperature equilibrium; conditioning steam of appropriate quality; time minimized before sterilisation.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.76	§8.76	**Is each EO cycle monitored with BIs at worst-case locations?** **Expected outcome:** Appropriate number of BI test units distributed at validated worst-case locations.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.77	§8.77	**Are EO critical process parameters controlled?** **Expected outcome:** EO concentration, pressure, amount of gas, relative humidity, temperature and exposure time considered in validation and routine monitoring.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.78	§8.78	**Is EO aeration validated?** **Expected outcome:** Load aerated to desorb EO/reaction products to predetermined levels; aeration phase validated within overall EO validation.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.79	§8.79	**Is sterile filtration performed with a validated ≤0.22 µm filter?** **Expected outcome:** Solutions filtered through a sterile sterilising grade filter (max 0.22 µm nominal) validated for a sterile filtrate, then aseptically filled; filter compatible and per the marketing authorisation.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.80	§8.80	**Are prefilters/additional sterilising filters used per the CCS?** **Expected outcome:** Bioburden-reduction prefilters and/or sterilising filters used to control bioburden; an additional sterilising filter near the point of fill considered in the CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.81	§8.81	**Is the filtration system selection justified and documented?** **Expected outcome:** Components/arrangement based on product CQAs; minimize fibres/particles/impurities; filter compatible with the fluid; adsorption and extractables/leaching evaluated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.82	§8.82	**Is the filtration system designed to required criteria?** **Expected outcome:** Operates within validated parameters; maintains filtrate sterility; minimizes aseptic connections; allows cleaning/SIP; permits in-place integrity testing of the final 0.22 µm filter before and after filtration.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.83	§8.83	**Is sterile filtration validated per Pharmacopeia?** **Expected outcome:** Validated per relevant Pharmacopeia under worst-case conditions; grouping by strength/variation justified and documented.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.84	§8.84	**Is bacterial retention testing appropriately performed?** **Expected outcome:** Wherever possible using the product to be filtered (or a justified surrogate); challenge organism justified.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.85	§8.85	**Are filtration parameters established during validation?** **Expected outcome:** Wetting fluid and integrity-test value; pre-filtration hold time, conditioning, max filtration time, max operating pressure, flow rate, max volume, temperature and pressure difference established.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.86	§8.86	**Are routine filtration controls and records maintained?** **Expected outcome:** Adherence to validated parameters; critical parameters (e.g. min filtration time, pressure difference) recorded in the batch record; significant deviations documented and investigated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.87	§8.87	**Is filter integrity verified pre-use (PUPSIT) and post-use?** **Expected outcome:** Pre-use post-sterilisation integrity test (PUPSIT) and a non-destructive post-use test performed; validated and correlated to microbial retention; a risk-assessed alternative applied only where PUPSIT is not possible.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.88	§8.88	**Are critical gas/air vent filters integrity tested after use?** **Expected outcome:** Critical vent filters linked to product sterility verified by post-use testing in situ.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.89	§8.89	**Are non-critical vent filters integrity-confirmed at intervals?** **Expected outcome:** Confirmed and recorded at appropriate intervals; extended-use filters tested at installation and before replacement; maximum duration specified and monitored.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.90	§8.90	**Is unintended wetting of gas filters avoided?** **Expected outcome:** Unintended moistening/wetting of gas filters or equipment avoided.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.91	§8.91	**Are multi-filter sterilising systems fully integrity tested?** **Expected outcome:** A validated multi-filter sterilising system is treated as one unit; all filters pass post-use integrity testing.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.92	§8.92	**Is redundant filtration integrity handled correctly?** **Expected outcome:** Post-use integrity test of the primary filter; if integral, the redundant filter test is not required; if the primary fails, the redundant filter is tested with investigation/risk assessment.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.93	§8.93	**Are bioburden samples taken correctly for filtration?** **Expected outcome:** From the bulk and immediately before the final sterile filtration (before the first filter in redundant set-ups); sampling designed to avoid contamination.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.94	§8.94	**Are liquid sterilising filters discarded appropriately?** **Expected outcome:** Discarded after a single batch; not used for more than one working day unless such use is validated.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.95	§8.95	**Is campaign filter use justified and controlled?** **Expected outcome:** Risks of filter-use duration assessed/documented; validation shows no compromise to performance/filtrate; maximum validated duration documented with controls; contaminated/defective filters removed.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.96	§8.96	**Are FFS environmental conditions compliant?** **Expected outcome:** Terminally sterilised FFS per §8.3/8.4; aseptic FFS per §8.10.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.97	§8.97	**Is FFS packaging-film contamination controlled?** **Expected outcome:** Films meet defined specifications (thickness/strength, microbial/particulate, integrity, artwork); bioburden/endotoxin defined and controlled in the PQS/CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.98	§8.98	**Is FFS equipment operation understood and validated?** **Expected outcome:** Set-up, filling, sealing and cutting understood so critical parameters are validated, controlled and monitored.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.99	§8.99	**Are FFS product-contact gases filtered and verified?** **Expected outcome:** Filtered as close to point of use as possible; gas quality and filtration effectiveness verified periodically per §6.18/6.19.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.100	§8.100	**Are FFS qualification controls aligned with the CCS?** **Expected outcome:** Critical-zone boundaries, EM (machine and background), gowning, integrity testing, campaign duration, film control, CIP/SIP and machine/alarm management addressed.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.101	§8.101	**Are FFS critical process parameters determined?** **Expected outcome:** Dimensions/cutting, forming temperatures/times/pressures, sealing temperatures/uniformity/times/pressures, environmental/product temperature, seal strength testing, filling volumes/speeds and printing/embossing controlled.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.102	§8.102	**Are FFS CPP verified, monitored and recorded in production?** **Expected outcome:** Appropriate procedures applied during production.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.103	§8.103	**Are FFS forming/sealing issues detected and rectified?** **Expected outcome:** Procedures describe detection/rectification; rejected units or sealing issues recorded and investigated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.104	§8.104	**Is FFS maintenance risk-based with tooling inspection?** **Expected outcome:** Maintenance/inspection plans for tooling critical to sealing; quality concerns documented and investigated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.105	§8.105	**Is terminally sterilised BFS installed in the correct environment?** **Expected outcome:** BFS for terminally sterilised products in at least grade D; point of fill per §8.3/8.4.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.106	§8.106	**Are BFS aseptic environmental conditions met?** **Expected outcome:** Shuttle-type: parison-open areas meet grade A at critical zones; rotary-type: filling environment within the parison meets grade A; equipment in at least grade C with grade A/B clothing and risk-based operator monitoring.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.107	§8.107	**Is BFS total particle monitoring approached correctly?** **Expected outcome:** In-operation total particle monitoring not expected; design data demonstrate critical zones meet grade A in operation.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.108	§8.108	**Is BFS viable monitoring risk-based and continuous where feasible?** **Expected outcome:** Designed per section 9; in-operation viable monitoring for the full duration of critical processing (rotary critical-zone limitation acknowledged).	☐ C ☐ NC ☐ OBS ☐ N/A	
8.109	§8.109	**Does BFS EM account for airflow and heat?** **Expected outcome:** Considers moving parts, complex airflow and high heat (e.g. airflow visualisation), air-filter configuration/integrity, cooling integrity and equipment design/qualification.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.110	§8.110	**Are BFS container-contact gases filtered and verified?** **Expected outcome:** Air/gases contacting critical container surfaces appropriately filtered; quality/effectiveness verified periodically per §6.18/6.19.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.111	§8.111	**Is BFS polymer granulate contamination prevented?** **Expected outcome:** Prevented by appropriate design, control and maintenance of granulate storage, sampling and distribution.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.112	§8.112	**Is BFS extrusion sterility assurance validated?** **Expected outcome:** Extrusion capability to provide sterility assurance understood and validated; polymer bioburden/endotoxin defined/controlled in PQS/CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.113	§8.113	**Are BFS interventions requiring cessation/re-sterilisation defined?** **Expected outcome:** Clearly defined in the filling procedure and included in the APS as relevant.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.114	§8.114	**Are BFS qualification controls aligned with the CCS?** **Expected outcome:** Critical-zone boundaries, EM, gowning, integrity testing, campaign duration, granulate/extrusion temperature control, CIP/SIP and machine/alarm management addressed.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.115	§8.115	**Are BFS critical process parameters determined?** **Expected outcome:** CIP/SIP, extrusion parameters/temperatures, mould temperatures/cooling, ancillary component preparation/sterilisation, EM, wall thickness, filling volumes/speeds, printing, 100% integrity testing and flash removal controlled.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.116	§8.116	**Are BFS CPP verified, monitored and recorded?** **Expected outcome:** Appropriate procedures applied during production.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.117	§8.117	**Are BFS blowing/forming/sealing issues detected and rectified?** **Expected outcome:** Procedures describe detection/rectification; rejected units/sealing issues recorded and investigated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.118	§8.118	**Is BFS component addition controlled?** **Expected outcome:** Components decontaminated and added via a clean/controlled process; aseptic additions under grade A with pre-sterilised components; terminal processes ensure sterility of all pathways; sealing validated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.119	§8.119	**Is BFS maintenance risk-based for sealing/integrity/sterility?** **Expected outcome:** Maintenance/inspection plans for items critical to unit sealing, integrity and sterility.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.120	§8.120	**Are BFS moulds treated as critical equipment?** **Expected outcome:** Mould changes/modifications trigger container integrity assessment and, where indicated, validation; issues documented and investigated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.121	§8.121	**Is lyophilization treated as an extension of aseptic processing?** **Expected outcome:** Equipment/processes designed to maintain product sterility from filling of lyophilization product to completion; controls determined by the CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.122	§8.122	**Is lyophilizer sterilisation validated and hold time challenged?** **Expected outcome:** Lyophilizer/associated equipment sterilisation validated; hold time between sterilisation and use challenged in APS; regular sterilisation; re-sterilisation after maintenance/cleaning; protection after sterilisation.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.123	§8.123	**Are lyophilizers designed to minimize intervention with justified sterilisation frequency?** **Expected outcome:** Loading/unloading minimizes operator intervention; manual/no-barrier lyophilizers sterilised before each load; automated/closed-barrier systems' frequency justified/documented in the CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.124	§8.124	**Is lyophilizer integrity maintained and tested?** **Expected outcome:** Integrity maintained after sterilisation and during lyophilization; filter sterilised before each use with integrity results in batch release; vacuum/leak integrity testing frequency documented and maximum leakage checked each cycle.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.125	§8.125	**Are lyophilization trays checked regularly?** **Expected outcome:** Checked to ensure they are not misshapen or damaged.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.126	§8.126	**Is lyophilizer loading/unloading designed to protect product?** **Expected outcome:** Documented loading pattern; grade A transfer of partially closed containers with minimized intervention; airflow not adversely affected; unsealed containers protected by barrier; grade A maintained where stoppers not seated; sterile utensils.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.127	§8.127	**Do closed systems reduce contamination and manual manipulation?** **Expected outcome:** Designed to reduce the need for manual manipulations and associated risks.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.128	§8.128	**Is sterility of closed-system product-contact surfaces ensured?** **Expected outcome:** Product-contact surface sterility ensured; connection to the sterilised pathway after the final filter designed to be made aseptically (e.g. intrinsic devices).	☐ C ☐ NC ☐ OBS ☐ N/A	
8.129	§8.129	**Is integrity of aseptic connection components ensured?** **Expected outcome:** Measures ensure component integrity, captured in the CCS; integrity tests considered where sterility risk exists; supplier failure-mode data collated.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.130	§8.130	**Is the closed-system background environment appropriate?** **Expected outcome:** Based on design/process; grade A where integrity may be compromised; lower grade if demonstrated integral each usage; transfers between grades assessed; opening performed in an appropriate grade or with further cleaning/disinfection/sterilisation.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.131	§8.131	**Are single-use systems designed to reduce manipulation?** **Expected outcome:** SUS designed to reduce manipulations and complexity of manual interventions.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.132	§8.132	**Are SUS-specific risks assessed in the CCS?** **Expected outcome:** Product/contact interactions, fragility, increased manual operations/connections, assembly complexity, filter pre/post-use integrity, holes/leakage, opening risk and particle contamination assessed.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.133	§8.133	**Is SUS sterilisation validated?** **Expected outcome:** Validated and shown to have no adverse impact on system performance.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.134	§8.134	**Are SUS suppliers assessed and sterility verified?** **Expected outcome:** Supplier assessment (incl. sterilisation) critical; sterility assurance verified at supplier qualification; evidence of sterilisation of each unit checked on receipt.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.135	§8.135	**Is SUS adsorption/reactivity evaluated?** **Expected outcome:** Adsorption and reactivity of product with contact surfaces evaluated under process conditions.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.136	§8.136	**Are SUS extractable/leachable profiles evaluated?** **Expected outcome:** Profiles evaluated (especially polymer-based), per component; high-risk leachables assessed including safety; simulated conditions reflect actual processing.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.137	§8.137	**Do SUS maintain integrity throughout processing?** **Expected outcome:** Integrity maintained under intended conditions; structural integrity under extreme conditions (e.g. freeze/thaw, transport); intrinsic sterile connection integrity verified.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
8.138	§8.138	**Are SUS acceptance criteria and receipt checks in place?** **Expected outcome:** Acceptance criteria per risk/criticality; each SUS checked on receipt against approved specification; visual inspection of packaging/label and review of documents (CoC, proof of sterilisation) performed and documented before use.	☐ C ☐ NC ☐ OBS ☐ N/A	
8.139	§8.139	**Are critical manual SUS handling operations verified in APS?** **Expected outcome:** Assembly and connections subject to appropriate controls and verified during APS.	☐ C ☐ NC ☐ OBS ☐ N/A	

Section 9 — Environmental & Process Monitoring

Status key: C = Compliant · NC = Non-compliant · OBS = Observation (note in evidence column) · N/A = Not applicable. *Mark the box and record supporting evidence, gaps or CAPA reference alongside.*

#	Ref	Audit question / expected outcome	Status	Observation & evidence
9.1	§9.1	**Is the EM/process monitoring programme part of the CCS?** **Expected outcome:** Programme monitors controls; the reliability of viable, non-viable and APS elements is limited individually but together confirms system reliability.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.2	§9.2	**Does the programme comprise the required elements?** **Expected outcome:** Total particle EM; viable environmental and personnel monitoring; temperature/RH and specific characteristics; APS (aseptic product).	☐ C ☐ NC ☐ OBS ☐ N/A	
9.3	§9.3	**Is monitoring information used for release and periodic assessment?** **Expected outcome:** Used for routine batch certification/release and periodic assessment/investigation, for both terminal and aseptic processes.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.4	§9.4	**Is a documented, risk-based EM programme established?** **Expected outcome:** Purpose defined; risk assessments set locations, frequency, methods and incubation; critical monitoring locations determined; reviewed regularly within the CCS/trend context.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.5	§9.5	**Is routine monitoring performed in operation throughout critical stages?** **Expected outcome:** Cleanrooms, clean air equipment and personnel monitored in operation throughout all critical stages including set-up.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.6	§9.6	**Are temperature/RH and other characteristics controlled?** **Expected outcome:** Controlled within ranges aligned with product/process/personnel requirements and cleanliness standards.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.7	§9.7	**Does grade A monitoring demonstrate maintained aseptic conditions?** **Expected outcome:** Monitoring at the highest-risk locations; sampling device selection/orientation/positioning justified to obtain reliable critical-zone data.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.8	§9.8	**Do sampling methods avoid contamination risk?** **Expected outcome:** Sampling methods pose no risk of contamination to operations.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.9	§9.9	**Are alert levels and action limits set for viable and total particle?** **Expected outcome:** Set per Tables 5 & 6 (or tighter per data/process/CCS); alert levels based on qualification results and periodically reviewed on trend data.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.10	§9.10	**Are alert levels set to detect adverse trends?** **Expected outcome:** Grade A (total particle), B, C and D alert levels detect and address adverse trends/deterioration.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
9.11	§9.11	**Is a trending approach defined?** **Expected outcome:** Trends include increasing/consecutive excursions, common-cause isolated excursions and changes in flora type/numbers (with attention to spore-formers/moulds).	☐ C ☐ NC ☐ OBS ☐ N/A	
9.12	§9.12	**Is grade C/D in-operation monitoring based on data?** **Expected outcome:** Based on qualification and routine data enabling trend analysis; action limits may be tighter than Tables 5 & 6 depending on operations.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.13	§9.13	**Are exceedances of action/alert levels actioned?** **Expected outcome:** Action limit exceedances trigger root-cause investigation, product impact assessment and CAPA; alert level exceedances trigger assessment/follow-up.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.14	§9.14	**Is a total particle monitoring programme established?** **Expected outcome:** Established to assess contamination risks and maintain a qualified state for sterile operations.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.15	§9.15	**Are airborne particle limits applied per Table 5?** **Expected outcome:** Limits for each graded area per Table 5.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.16	§9.16	**Is grade A particle monitoring for the full duration of critical processing?** **Expected outcome:** Undertaken for the full duration including equipment assembly.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.17	§9.17	**Is grade A continuously monitored at an adequate flow rate?** **Expected outcome:** Continuous monitoring (≥0.5 and ≥5 µm) at ≥28 L/min so interventions/transient events/deterioration are captured; each result correlated with alert/action limits; alarms on alert.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.18	§9.18	**Is grade B monitored with a similar system?** **Expected outcome:** Similar system with possibly reduced frequency but capturing increased contamination/deterioration; alarms on alert.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.19	§9.19	**Does the monitoring system account for material hazards?** **Expected outcome:** Considers risks from live organisms, powders or radiopharmaceuticals (biological/chemical/radiation hazards).	☐ C ☐ NC ☐ OBS ☐ N/A	
9.20	§9.20	**Are contaminant-present processes monitored to assure classification?** **Expected outcome:** Strategy assures classification before and after exposure; increased viable monitoring; monitoring during simulated operations at appropriate intervals per CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.21	§9.21	**Are automated sample volumes justified?** **Expected outcome:** Sample size (a function of sampling rate) need not match classification volumes but is justified.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
9.22	§9.22	**Is aseptic viable monitoring frequent and justified?** **Expected outcome:** Combination of settle plates, volumetric air, glove/gown/surface sampling; methods justified in the CCS and shown not to impact grade A/B airflow; surfaces monitored at end of operations.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.23	§9.23	**Is viable monitoring performed outside normal operations?** **Expected outcome:** Performed when not manufacturing (post-disinfection, pre-start, batch completion, after shutdown) and in unused associated rooms; additional locations after incidents.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.24	§9.24	**Is continuous viable air monitoring performed in grade A?** **Expected outcome:** For the full duration of critical processing including aseptic set-up; a similar approach considered for grade B; interventions/transient events captured.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.25	§9.25	**Is personnel monitoring risk-based and after critical interventions?** **Expected outcome:** Locations/type/frequency by risk; sampling at intervals and after critical interventions and on each exit from grade B; gloves/gowns replaced after monitoring where required.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.26	§9.26	**Is grade A/B personnel microbial monitoring performed?** **Expected outcome:** Performed, with enhanced emphasis on gowns for manual operations, justified in the CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.27	§9.27	**Is routine monitoring by production staff overseen by QA?** **Expected outcome:** Subject to regular quality-unit oversight.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.28	§9.28	**Are rapid/alternative monitoring methods considered?** **Expected outcome:** Considered to expedite detection; adopted only after validation demonstrating equivalence/superiority.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.29	§9.29	**Are sampling methods understood with recovery data?** **Expected outcome:** Methods/equipment understood; procedures for operation/interpretation; recovery-efficiency data available.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.30	§9.30	**Are viable action limits applied per Table 6?** **Expected outcome:** Action limits for viable contamination per Table 6.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.31	§9.31	**Are grade A/B organisms identified to species?** **Expected outcome:** Identified to species with impact evaluation; grade C/D identification considered where limits/levels exceeded or indicative organisms isolated.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.32	§9.32	**Is APS used to verify (not primarily validate) the aseptic process?** **Expected outcome:** Periodic verification using sterile media/surrogate; not the primary means of validation; media/surrogate selected to imitate product characteristics; alternatives for indirect-impact processes.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
9.33	§9.33	**Does APS imitate the routine process including all critical steps?** **Expected outcome:** Assesses all aseptic operations to container sealing; non-filterable additional steps; inert gas substituted with air unless anaerobic intended; sterile-powder surrogates; no separated unit-operation simulations without justification; lyophilization chain represented; viability-affecting steps avoided.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.34	§9.34	**Does APS include representative manipulations and worst cases?** **Expected outcome:** Inherent/corrective interventions performed at routine-like manner/frequency; inclusion/frequency based on assessed risks to product sterility.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.35	§9.35	**Is APS prevented from justifying unnecessary risks?** **Expected outcome:** APS not used to justify practices posing unnecessary contamination risks.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.36	§9.36	**Is the APS plan developed with required considerations?** **Expected outcome:** Worst-case conditions/variables, representative container/closure sizes, max holding times, adequate fill volume, inert-gas substitution, growth-supporting media, reliable detection, sufficient duration, shift factors, interruptions, EM throughout, campaign start/end and any end-of-campaign APS justified in the CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.37	§9.37	**For sterile active substances, is APS representative?** **Expected outcome:** Batch size represents routine operation and simulates worst-case interventions covering all product-contact surfaces; simulated materials subjected to microbial evaluation without compromising recovery.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.38	§9.38	**Is APS validated and revalidated at required frequency?** **Expected outcome:** Initial validation with at least three consecutive satisfactory runs covering all shifts; after significant modifications; normally repeated ~twice a year per aseptic process/line/shift; each operator participates in at least one successful APS annually.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.39	§9.39	**For manual operations, is APS operator-specific?** **Expected outcome:** Each operator initially validated with at least 3 consecutive successful APS per container/closure/equipment train and revalidated ~every 6 months; batch size mimics routine.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.40	§9.40	**Is the number of APS units sufficient?** **Expected outcome:** Sufficient to simulate all representative activities; typically 5,000–10,000 units; for batches under 5,000 units, APS at least equals the production batch size; justification captured in the CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.41	§9.41	**Are APS units handled and incubated correctly?** **Expected outcome:** Units agitated/swirled/inverted before incubation; all integral units incubated (incl. cosmetic defects/non-destructive checks); discarded units comparable to routine and not exceeding routine clearance.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.42	§9.42	**Are discarded product-contact materials simulated?** **Expected outcome:** Discarded materials (e.g. product flushes) simulated with media and incubated unless demonstrated not to impact sterility.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
9.43	§9.43	**Are APS units incubated for visual detection?** **Expected outcome:** Incubated in clear containers (or identical clear substitutes; or a validated detection method); isolated organisms identified to species where practical.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.44	§9.44	**Is APS incubation prompt and justified?** **Expected outcome:** Incubated without unnecessary delay; incubation conditions/duration scientifically justified and validated for detection sensitivity.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.45	§9.45	**Is APS completion inspection and positive control performed?** **Expected outcome:** Inspected by trained/qualified personnel under suitable conditions; samples positive-controlled with reference organisms and representative local isolates.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.46	§9.46	**Is the APS acceptance criterion zero growth with defined failure response?** **Expected outcome:** Target zero growth; any contaminated unit fails the APS, triggering root-cause investigation, CAPA, ≥3 successful consecutive repeats, review of production since the last successful APS, quarantine of affected product, operator activity limits and resumption only after successful revalidation.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.47	§9.47	**Are APS runs fully documented with reconciliation?** **Expected outcome:** Full documentation with reconciliation of units (filled/incubated/not incubated with justification); all interventions recorded with start/end time and person; monitoring/testing data in the APS batch record.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.48	§9.48	**Is an aborted APS handled per procedure?** **Expected outcome:** Aborted only where written procedures require commercial lots to be equally handled; investigation documented.	☐ C ☐ NC ☐ OBS ☐ N/A	
9.49	§9.49	**Is the aseptic process re-validated when triggered?** **Expected outcome:** Repeat of initial validation when idle for an extended period or on changes to process/equipment/procedures/environment or new container/closure combinations.	☐ C ☐ NC ☐ OBS ☐ N/A	

Section 10 — Quality Control (QC)

Status key: C = Compliant · NC = Non-compliant · OBS = Observation (note in evidence column) · N/A = Not applicable. *Mark the box and record supporting evidence, gaps or CAPA reference alongside.*

#	Ref	Audit question / expected outcome	Status	Observation & evidence
10.1	§10.1	**Are QC personnel appropriately trained and experienced?** **Expected outcome:** Personnel with training/experience in microbiology and sterility assurance support manufacturing design, EM regime and investigations of microbiologically-linked events.	☐ C ☐ NC ☐ OBS ☐ N/A	
10.2	§10.2	**Do specifications include microbial/particulate/endotoxin limits?** **Expected outcome:** Raw material, component and product specifications include such limits where indicated by monitoring and/or the CCS.	☐ C ☐ NC ☐ OBS ☐ N/A	
10.3	§10.3	**Is a bioburden assay performed each batch with defined limits?** **Expected outcome:** Performed each batch (aseptic and terminal), considered at batch review; defined limits before the final filter/terminal sterilisation with worst-case sampling; overkill-cycle bioburden monitored at scheduled intervals.	☐ C ☐ NC ☐ OBS ☐ N/A	
10.4	§10.4	**For parametric release, is a pre-sterilisation bioburden programme in place?** **Expected outcome:** Programme with per-batch bioburden assay; worst-case sampling; organisms identified with impact determined; endotoxin/pyrogen monitored where appropriate.	☐ C ☐ NC ☐ OBS ☐ N/A	
10.5	§10.5	**Is the sterility test treated as the last of a series of controls?** **Expected outcome:** Regarded as the last of a series of critical controls; cannot assure sterility of product not meeting design/procedural/validation parameters; validated for the product concerned.	☐ C ☐ NC ☐ OBS ☐ N/A	
10.6	§10.6	**Is sterility test sampling representative and risk-based?** **Expected outcome:** Performed aseptically; samples represent the whole batch including highest-risk parts (aseptic batch start/end and post-critical-intervention; worst-case load locations; different lyophilization loads); sub-batch testing where applicable.	☐ C ☐ NC ☐ OBS ☐ N/A	
10.7	§10.7	**Are short-shelf-life products managed for release?** **Expected outcome:** Where a sterility result is not available before release, additional process design, monitoring and/or alternative methods are assessed and documented.	☐ C ☐ NC ☐ OBS ☐ N/A	
10.8	§10.8	**Does sample decontamination not impact test sensitivity?** **Expected outcome:** Any external decontamination of sterility samples (e.g. VHP, UV) does not negatively impact test sensitivity or sample reliability.	☐ C ☐ NC ☐ OBS ☐ N/A	
10.9	§10.9	**Is media quality control/growth promotion testing performed?** **Expected outcome:** Product-test media QC-tested per Pharmacopeia; EM/APS media growth-promotion tested before use with a justified reference set and local isolates; normally performed by the end user; outsourcing justified with transport/shipping considered.	☐ C ☐ NC ☐ OBS ☐ N/A	

#	Ref	Audit question / expected outcome	Status	Observation & evidence
10.10	§10.10	**Is EM/trend data reviewed at batch release with OOS/OOT procedures?** **Expected outcome:** EM and trend data for classified areas reviewed at certification/release; written procedure for out-of-trend/limit data; short-shelf-life products review recent data and consider rapid methods.	☐ C ☐ NC ☐ OBS ☐ N/A	
10.11	§10.11	**Are rapid/automated microbial methods validated?** **Expected outcome:** Validated for the products or processes concerned where used for general manufacturing purposes.	☐ C ☐ NC ☐ OBS ☐ N/A	