

BUYER DUE DILIGENCE

Lyophilized Product CMO Due-Diligence Checklist

A public, non-confidential framework for evaluating whether a defined sterile lyophilized product, process, presentation and evidence package can be transferred and governed at a proposed manufacturing site.

Three questions before comparing sites

01	Is the product sufficiently understood? Clarify formulation, critical quality attributes, thermal behavior, container-closure system, process history, analytical status and target product profile.
02	Can the product fit the proposed equipment and sterile route? Connect filling, loading, freezing, primary and secondary drying, stoppering, unloading and inspection to the actual manufacturing train.
03	Can the transfer be proven through stage-gated evidence? Define gaps, methods, cycle rationale, scale-up risks, engineering work, validation strategy, acceptance criteria and lifecycle governance.

Eight-point checklist

Checkpoint	What the buyer should establish	Checkpoint	What the buyer should establish
1. Product knowledge	Formulation, thermal behavior, stability, critical quality attributes and known sensitivities.	5. Container-closure fit	Vial, stopper, fill volume, headspace, stoppering, container-closure integrity and handling risks.
2. Sterile-process integration	Filling, interventions, transfer, loading, stoppering and unloading within the sterility-assurance system.	6. Analytical readiness	Methods, transfer status, reference standards, moisture, potency, impurities, sterility and relevant physical attributes.
3. Cycle understanding	Freezing, primary drying, secondary drying, critical parameters, endpoint logic and product-temperature limits.	7. Transfer and validation	Gap assessment, protocol, engineering batches, comparability, PPQ/validation route and acceptance criteria.
4. Equipment and scale fit	Shelf area, condenser capacity, refrigeration, vacuum, control-system capability and scale-dependent heat/mass transfer.	8. Quality and supply governance	Responsibilities, change control, deviations, release, materials, continuity and lifecycle monitoring.

Decision principle: a listed lyophilization platform or equipment match does not establish project suitability. The decision must connect product knowledge, sterile-process integration, cycle evidence, scale, analytical readiness and target-market requirements.

PRODUCT-TO-CYCLE EVIDENCE

Questions to take into technical due diligence

01 Formulation and thermal behavior Ask: What evidence defines the product's freezing behavior, collapse or critical temperature, moisture target and degradation risks? Evidence examples: development history, thermal analysis, formulation rationale, stability trends and risk assessments	02 Freezing strategy Ask: How are nucleation, supercooling, freezing rate, phase behavior and hold times controlled or justified? Evidence examples: cycle development records, product-temperature data, equipment capability and batch observations
03 Primary drying Ask: How are shelf temperature, chamber pressure, heat transfer, mass transfer, endpoint and product-temperature limits defined? Evidence examples: engineering studies, product and equipment data, endpoint evidence, scale-up rationale and acceptance ranges	04 Secondary drying Ask: How are bound moisture, residual moisture, desorption conditions, duration and product quality connected? Evidence examples: cycle studies, moisture method, stability data, process ranges and release strategy
05 Sterile interfaces Ask: How are filling, interventions, loading, stoppering, unloading and container closure integrated with contamination control? Evidence examples: process simulation strategy, intervention catalogue, transfer paths, environmental monitoring and CCI plan	06 Scale and transfer Ask: Which product and equipment differences could change heat/mass transfer, cycle duration, uniformity or critical quality attributes? Evidence examples: gap assessment, scale-up model, engineering-batch plan, comparability protocol and stage gates

Transfer boundary: do not treat the donor cycle as a set of values to copy. Transfer should preserve the product and process rationale while accounting for equipment geometry, control capability, loading pattern, vial heat-transfer conditions and the receiving site's sterility-assurance system.

Red flags that require deeper evidence

- A cycle recipe is available, but its product and process rationale is not understood.
- Equipment differences are described as minor without a documented heat- and mass-transfer assessment.
- Aseptic filling and loading/unloading interfaces are reviewed separately from lyophilization.
- Moisture, appearance, potency, impurities or reconstitution behavior are not linked to cycle ranges.
- The schedule assumes immediate validation without a justified development and engineering-batch route.
- Sensitive formulas, process parameters or dossiers are requested before controlled confidentiality is in place.

CONTROLLED PROJECT PATH

From non-confidential screen to transfer readiness

01	Public fit screen Confirm legal entity, site, public dosage-form scope, target market and non-confidential project objective.
02	Confidentiality and scope Agree purpose, permitted use, access, disclosure controls and review responsibilities.
03	Product and cycle gap assessment Compare formulation knowledge, cycle rationale, methods, equipment, scale and sterile-process interfaces.
04	Development and engineering route Define studies, batches, analytical evidence, acceptance criteria, decision rights and escalation.
05	Validation and regulatory readiness Connect process validation, sterility assurance, comparability, dossier impact and quality agreements.
06	Commercial and lifecycle governance Confirm release, change control, supply continuity, trending, stability and post-transfer ownership.

Non-confidential information for the first discussion

- Dosage form, presentation, container-closure system and high-level product characteristics
- Development/commercial stage, available cycle history and proposed cooperation model
- Target market, dossier status, regulatory objective and intended timing
- Indicative batch-size range, fill volume and supply objective
- The specific formulation, cycle, scale-up, analytical, transfer or supply decision to be resolved

Information boundary: do not send patient information, prescriptions, complete formulas, detailed cycle parameters, unpublished dossiers or trade secrets before an appropriate confidentiality arrangement. An initial discussion does not confirm project acceptance, capacity, price, regulatory outcome or service commitment.

Discuss a non-confidential lyophilized-product project fit

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Authoritative references

1. WHO TRS 1044, Annex 2 - GMP for sterile pharmaceutical products
2. U.S. FDA - Sterile Drug Products Produced by Aseptic Processing - CGMP
3. WHO TRS 1044, Annex 4 - Technology transfer in pharmaceutical manufacturing
4. NMPA - Contract-manufacturing supervision requirements

This checklist is a public business decision aid. It is not medical, legal or regulatory advice, and it is not a certification, approval, audit outcome or conclusion about any facility. Project suitability must be verified for the defined product, site, process, market and current records.