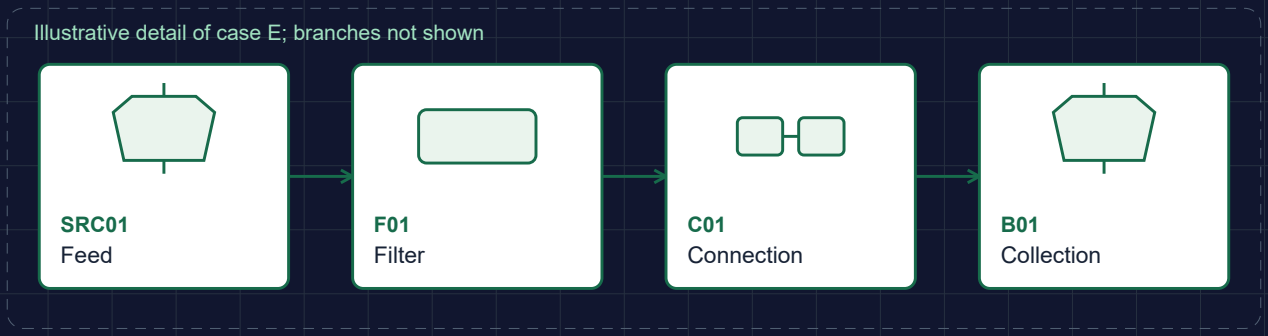
PHARMA ENGINEERING

Single-Use & Bioprocess Systems

GMP Guide and Operational Toolkit

TECHNICAL GUIDE · EDITABLE TOOLS



Rev.1.0 · October 2026

GuideGxP

www.guidegxp.com

Edition, scope and responsibilities

Single-Use & Bioprocess Systems — GMP guide and operational toolkit. Rev. 1.0, October 2026. This edition uses sources verified up to 10 October 2026. References indicate their status on the verification date: before using a conclusion in a real project, the site owner checks the applicable version and any updates.

Ref. GuideGxP — original operational method

This guide helps users develop reasoned decisions about single-use systems employed in bioprocesses for human medicines. It covers intended use, requirements, performance, fluid paths, materials, integrity, sterilisation, qualification, operational control and lifecycle management. The starting point is the product and manufacturing stage: a process-contact equipment part, an ingredient and a final container serve different functions and do not automatically receive the same regulatory classification.

Ref. EudraLex Volume 4; 21 CFR Part 211; 21 CFR 210.3

The treatment of GMP distinguishes sterile processing from upstream activities. Annex 1 concerns the manufacture of sterile medicinal products; adopting its principles for non-sterile products requires an identified, documented application. Using a bag or connection described as sterile does not, by itself, extend that status to the entire process.

Ref. EU GMP Annex 1; EU GMP Annex 2

The discussion focuses on decisions about the single-use system. Water and WFI, HVAC, CIP/SIP and other permanent installations are considered at their interfaces. This guide does not develop a complete final-packaging validation, a complete viral-safety strategy, a complete APS programme or an assessment of local waste and biosafety legislation. Each interface owner documents the necessary further work and the point at which responsibility passes to another site process.

Ref. GuideGxP — original operational method; EU GMP Annex 15; EU GMP Annex 2

The toolkit provides working documents to adapt to the recipient’s quality system. Completing a form does not constitute qualification, authorisation for use, demonstration of sterility or batch release. Responsibility for product quality and the pharmaceutical quality system remains with the organisation: technical competence, examination of evidence and approvals required by site procedures remain necessary.

Ref. EU GMP Chapter 1; ICH Q10; GuideGxP — original operational method

All cases are illustrative. Identities, quantities and results teach a line of reasoning and remain separate from site evidence. Example values must not be copied into acceptance-criterion fields. GuideGxP recommends leaving those fields blank until an authorised rationale has established the value, unit, source and range of applicability.

Ref. GuideGxP — original operational method

How to use the guide and toolkit

For a new application, start with chapters 1–4 and open TL-001. First define the product, stage, configuration and decision objective; select the tests only afterwards. For a change, read chapter 22 alongside the relevant technical chapter. For a problem observed during production, first preserve identities and records, then use chapter 23 without prejudging the cause.

Ref. GuideGxP — original operational method

Each chapter connects an operational question to a tool identified by a TL code. The primary tool number matches the chapter number. References to other tools help maintain consistency between, for example, the bill of materials, the materials assessment and change control. Not every template needs to be completed for every activity: the owner selects the relevant tools and documents exclusions.

Ref. GuideGxP — original operational method

From the question to a usable record

Step	Action	Result to retain
Define	State the question and assessment boundary.	Configuration, revision, stage and owner.
Collect	Open the cited documents and verify their identity and applicability.	References with revisions and the locations actually checked.
Assess	Compare data, assumptions and actual conditions.	Reasoned conclusion and questions that remain open.
Decide	Submit the package to the authorised role.	Decision, scope, conditions and signature or controlled approval.
Review	Identify the event or due date that requires reassessment.	Assigned action and traceability of the subsequent revision.

Ref. GuideGxP — original operational method

The Word templates suit specifications, plans, reviews, agreements and narrative records. The Excel templates organise repeated data, comparisons and calculations. Both formats separate the clean working version from the example. Master files bring together the tools of their respective format; modules allow users to open an individual tool. These are two ways of accessing the same 24 tools, rather than additional tools.

Ref. GuideGxP — original operational method

In Excel, yellow fields are for inputs and blue fields contain protected formulas. Protection prevents unintended changes: it is not a security system or spreadsheet validation. Before operational use, the file owner checks the inputs, units, applicable formulas, selected options and test result in accordance with site procedures.

Ref. GuideGxP — original operational method

A blank result may indicate missing data or a calculation outside its domain. Consult the associated status instead of replacing the blank with zero. Results describe checks on entered data: the file does not independently read a drawing, toxicology report or qualification. Where the template calls for a documented review, the reviewer examines the evidence, identifies its scope and records a conclusion.

Ref. GuideGxP — original operational method

To archive an actual use, create a copy with the identity required by the site and retain the distributed original. Record the template version alongside the documents and data used. Corrections, formula changes and template updates must be assessed within the local document system: replacing a file does not automatically update decisions already made.

Ref. GuideGxP — original operational method; EU GMP Chapter 4

Reading routes and levels of evidence

The six parts can be read in sequence or used as working routes. The table guides navigation; it does not automatically assign organisational responsibilities. The project identifies who prepares the information, who reviews it and who has the authority required to make the decision.

Ref. GuideGxP — original operational method

Choose the route from the decision to be made

Need	Chapters	Starting tools
Set up a new project	1–4; then 17 and 21	TL-001, TL-002, TL-004
Select and transfer a process stage	5–8; then 9–12	TL-005, TL-006, TL-008
Justify product contact and process protection	9 and 12–16; then 18	TL-009, TL-013, TL-015
Prepare qualification and production use	17–20; link 2, 9 and 21	TL-017, TL-018, TL-019
Assess a change or deviation	22–23 and the relevant technical chapter	TL-022, TL-023
Compare supply, availability and costs	3, 21 and 24	TL-003, TL-021, TL-024

Ref. GuideGxP — original operational method

Short citations alongside the blocks point to the source. Appendix B identifies the issuing body, version, nature and limitations of use. An official source may contain applicable requirements, GMP expectations, recommendations or information about the status of a revision: the context stated in the text must be retained when a sentence is reused in an internal document.

Ref. GuideGxP — original operational method; 21 CFR Part 211; FDA Aseptic Processing Guidance

Voluntary standards, pharmacopoeial chapters and industry protocols are presented within the limits of the public material actually verified. A catalogue or preview does not establish access to the complete licensed text and does not permit reconstruction of a proprietary procedure. Recipients obtain the version they need and assess its applicability when deciding to use it.

Ref. GuideGxP — original operational method

Drafts and concept papers are identified to help users follow developments in the technical framework. They do not replace texts in force at the source cut-off. GuideGxP proposals are working conventions intended to make the reasoning easier to follow: a checklist or indicator proposed by the guide does not thereby become an authority’s requirement.

Ref. GuideGxP — original operational method; EC — Chapter 4 / Annex 11 / Annex 22 consultation

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Part 01 / Chapter 01

Scope, intended use and responsibilities

Define the system to be governed, the manufacturing stage and the applicable framework. The reader prepares a scope suitable for approval that distinguishes the product, equipment, assembly and site responsibilities.

Related tools TL-001, TL-002, TL-004, TL-021

From component to process

A single-use system is not defined simply by identifying which parts are discarded after use. The starting point is the function the system performs in the process: containing a culture, preparing a solution, transferring an intermediate or receiving product after sterilising filtration. The conditions to be represented, the consequences of a defect and the evidence useful to the decision all change. This guide primarily concerns medicinal products for human use. Veterinary medicines, advanced therapies, medical devices and primary packaging require a specific assessment of their applicable framework.

Ref. EU GMP Annex 1; ICH Q7

Three objects often referred to simply as a “bag” need to be distinguished. The first is the supplied article with its own configuration. The second is the process-contact assembly, including connections, tubing and branches. The third is the integrated system, in which supports, instruments and operations enable use. If a bag instead serves as the final container, the regulatory question changes. A dossier prepared for process equipment does not automatically demonstrate the suitability of the container that will accompany the medicinal product to the patient.

Ref. EU GMP Annex 1; 21 CFR Part 211; ICH Q7

The distinction between the active substance, or drug substance, and the medicinal product, or drug product, should be recorded before sources are selected. A bioprocess passes through stages with different objectives; the fact that a stage precedes a sterile medicinal product does not turn every upstream operation into aseptic manufacture of a finished product. The description must identify what enters, what leaves and which state of the material is to be maintained. A generic expression such as “biologics facility” leaves precisely this information unresolved.

Ref. EU GMP Annex 1; ICH Q7

Within the US drug CGMP framework, component means an ingredient intended for use in manufacturing a drug. The definition in 21 CFR 210.3(b)(3) does not allow every piece of equipment to be treated as an ingredient. Provisions on ingredients, containers and closures apply when the object and its use genuinely fall into those categories. During document review, the term used by the supplier should therefore be compared with the actual function, avoiding the transfer of an acceptance procedure from one category to another merely because their names appear similar.

Ref. 21 CFR 210.3; 21 CFR Part 211

Applicability before the checklist

EU GMP Annex 1 governs the manufacture of sterile medicinal products. It allows selected principles to be adopted for non-sterile products as well, but those principles must be identified, documented and demonstrably applied. The choice should be understandable: which risk is to be addressed, which principle is adopted and what evidence verifies its implementation. Writing “Annex 1 applicable” for an entire upstream process, without distinguishing its stages, makes it difficult to understand which expectations are relevant and which instead represent additional site decisions.

Ref. EU GMP Annex 1

For biological manufacture within the scope of Annex 2, equipment, sampling, containment and the handling of single-use articles should be considered together in preventing contamination and cross-contamination. The boundary cannot stop at the liquid inside the bag: it also includes how the system is brought into the area, used and removed. Containment to protect people and the environment must be coordinated with product quality. Annex 2 is not a framework to apply indiscriminately to ATMPs, which remain outside its scope.

Ref. EU GMP Annex 2

At this edition’s evidence cutoff, 10 October 2026, the operative revision of Annex 15 is the 2015 version. For active substances, it constitutes optional supplementary guidance without adding requirements to EU GMP Part II. The 2026 concept paper and the related update are not an adopted revision. Those preparing a qualification plan should therefore distinguish the framework relevant to the process from the methodology the site chooses to use. A useful approach to organising the work does not, for that reason alone, become an additional Part II obligation.

Ref. EU GMP Annex 15; Annex 15 revision concept paper

The applicability matrix proposed by GuideGxP should also include a rationale for exclusions. “Out of scope” means that an activity is governed elsewhere, with an identifiable owner and document; it does not mean the risk does not exist. Water and WFI, HVAC and CIP/SIP remain interfaces when they serve the system under consideration. Similarly, this guide does not replace full assessments of the final container, viral clearance or local biosafety. The quality of the matrix depends on whether these links can be reconstructed without artificially expanding the single-use project.

Ref. GuideGxP — original operational method

Who retains responsibility

The pharmaceutical company retains responsibility for product quality and the effectiveness of the quality system, including outsourced activities and purchased materials. A supplier can perform studies, manufacture assemblies and provide reports; the site must still establish whether that evidence supports the intended use. This distinction is essential when a dossier appears complete: completeness of its contents list and suitability for the process are different assessments. The first check can identify missing documents; the second requires expertise in the product, configuration and actual conditions.

Ref. EU GMP Chapter 1; ICH Q10

GuideGxP proposes separating the technical decision, quality judgement and regulatory assessment in the brief. The process owner describes the function and conditions to be supported; technical functions assess the solution; Quality establishes how the conclusions enter the quality system; Regulatory assesses implications for the dossier and the jurisdiction concerned. These roles should not be copied as a universal organisational chart: the site assigns names, duties and delegated authority consistent with its own organisation. A useful signature identifies a specific decision, rather than merely participation in a meeting.

Ref. GuideGxP — original operational method; ICH Q10

An agreement with the supplier should make clear who performs the work, who makes the data available and who assesses deviations within the agreed scope. FDA guidance on quality agreements provides recommendations for contract manufacturing activities; it should not be presented as a new law or as a transfer of statutory responsibility. If a partner communicates a change, its technical judgement is an input to the assessment. Any use in the customer's process remains subject to the decisions assigned to the customer's own authorised functions.

Ref. FDA Quality Agreements Guidance; ICH Q10

The recommended working approach is to associate each open issue with an owner and the next decision required. An entry such as "check with supplier" does not clarify who should examine the document, which conditions should be compared or when the work can be considered complete. The brief should identify the person responsible for the request, the evidence reviewer and the authority that decides on use. Where these people belong to different functions, the handover must be explicit. Reaching an administrative deadline does not, by itself, resolve a technical uncertainty that remains documented.

Ref. GuideGxP — original operational method; ICH Q10

Reading source status

This edition distinguishes requirements, GMP expectations, official recommendations, voluntary standards, scientific observations and GuideGxP operational proposals. The classification helps the reader choose appropriate wording: it neither weakens a GMP expectation nor turns a voluntary standard into law. For each reference, the issuing body, version, scope and conditions of applicability need to be read. A generic declaration of compliance, without the edition adopted and the scope verified, does not allow the conclusion to be reconstructed. Catalogue documents substantiate what they state, not the content of clauses they do not make available.

Ref. GuideGxP — original operational method

The official public presentation of USP <665> expressly describes it as informational and not compendially applicable unless otherwise specified by regulatory authorities or enforcement bodies. Neither its number below one thousand nor the advertised official date of 1 May 2026 justifies a general claim that it is mandatory. Actual application requires the current authorised text and verification of the relevant authority's position. As of 10 October 2026, ICH Q3E remains a draft: proposed classes, SCTs, AETs and thresholds are not current requirements that can be inferred from the consultation alone.

Ref. USP <665> — public preview; ICH Q3E — EMA draft; ICH Q3E — FDA draft

PIC/S PI 006-4 has been current since 1 October 2026 and replaces PI 006-3; PE 009-18 is the current edition of the PIC/S guide at the same reference date. Implementation depends on the participating authority and does not automatically amend EU legislation or Annex 15. For standards, the current public reference for the specification, design, verification and application of SUS is ASTM E3051-25. Identifying the edition is not equivalent to demonstrating detailed compliance: this guide neither reproduces the proprietary text nor reconstructs it from the catalogue.

Ref. PIC/S PI 006-4; PIC/S PE 009-18 — publications index; ASTM E3051-25 — public scope

For ASME BPE, the publisher's catalogue lists BPE-2026, while the public contents link consulted leads to a 2024 preview. This guide therefore uses the reference only for the verified edition and scope context, without attributing 2026 clauses to the earlier contents page. The 2025 consultation on Chapter 4, Annex 11 and the new Annex 22 also remains draft material as of 10 October 2026: it does not replace the current versions. The project records the source actually adopted and plans an update check before decisions that depend on it.

Ref. ASME BPE-2026 — publisher catalogue; EC — Chapter 4 / Annex 11 / Annex 22 consultation; EudraLex Volume 4

A verifiable brief

TL-001 turns the scope into a verifiable brief. The product, stage and intended-use section states what the system will need to do and which state of the material it must support. The physical and functional boundary links to a revision-identified drawing showing inlets, outlets and branches. GuideGxP recommends completing these fields before requesting quotations: asking the market for a solution without defining the service leaves decisions that should belong to the site to the supplier and makes the subsequent comparison ambiguous.

Ref. GuideGxP — original operational method

In the applicability matrix, each row links jurisdiction, source, scope, rationale and reviewer. The person completing it should not fill every box with “applicable”: a reasoned selection is more useful than a list of acronyms. Excluded interfaces are entered in the dedicated table with their owner, governing document and residual risk. If a support, utility connection or operating step appears on the drawing but not in the brief, the reviewer must ask where it is governed. The Word template organises the question; it neither interprets the drawing nor independently discovers the omission.

Ref. GuideGxP — original operational method

The result feeds tools with different functions. TL-002 turns needs and boundaries into requirements and checks; TL-004 develops risk scenarios and uncertainty; TL-021 organises responsibilities and evidence at the supplier interface. The same text does not need to be rewritten in every file. What matters is preserving the reference to the current brief and explaining which decision is developed in the next document. When a stage or responsibility changes, these links allow the assessments requiring review to be identified, rather than distributing inconsistent versions of the same project.

Ref. GuideGxP — original operational method

Before approving the brief, the reviewer must also be able to describe what has not yet been decided. A gap may prevent production use while allowing a clarification request or a development comparison, provided the scope of that activity is defined. The outcome field therefore records the actual decision with its limits, actions and competent authority. GuideGxP recommends closing document review and authorisation for use separately: a readable brief creates the conditions for a decision, but does not demonstrate performance that has not yet been studied.

Ref. GuideGxP — original operational method

Worked case

Illustrative case Selvara: define the development scope before choosing the solution

Illustrative example: Selvara Biologics, the SB-M01 programme and all identifiers are fictional. The project concerns development of a monoclonal antibody drug substance using mammalian cells, in configuration SU-ASM-UP-01, revision A. The available data distinguish a seed working volume of 20 L, a production bioreactor working volume of 200 L and a separately measured harvest pool of 180 L. The process owner must prepare a brief to compare candidate configurations. None of these data constitutes authorisation to manufacture.

The first step is to assign a meaning to each volume. The 20 L and 200 L belong to different stages; the 180 L describe a subsequent pool and do not close a product balance. Writing “ninety per cent recovery” in the brief by deriving it from the latter two numbers would be an unsupported conclusion: a product mass basis and a complete balance are missing. The transition from seed to production does not establish a scaling law either. These qualifications prevent an initial description from becoming an unintended performance specification.

The process owner records that upstream processing is not being presented as sterile finished-product manufacture. Quality examines the drug-substance framework and the relevant contamination control principles, without inferring sterility from a closed bag. As a separate educational comparison, the transfer of medicinal product after the final filter in SU-CASE-E addresses a different question. That path includes an aseptic connection and a sterile receiving bag before filling; it is neither incorporated into the same intended-use statement nor used to assign characteristics to the SB-M01 process.

The boundary of SU-ASM-UP-01 is then linked to the interfaces already known: gas supply and exhaust, cooling and temperature control, electrical power and controls, upstream preparation and downstream transfer. The brief requires an owner for each, together with the document governing the external part. No individuals' names, verification reports or signed authorisations are supplied; those fields remain for the site to complete. The presence of the list does not prove that flow rates, signals or connection conditions are already suitable for the candidate configuration.

The useful decision is to begin comparing capacity and measurement conditions while keeping the missing control and measurement evidence visible. Engineering is tasked with making the interfaces verifiable in TL-002; the process owner must define the conditions to compare; Quality establishes the review pathway. Confirmation at the receiving scale remains necessary before conclusions can be drawn about transferred performance. The brief can thus describe a bounded development comparison without pretending that the candidate is already qualified or that a supplier dossier resolves every point.

The case ends with an understandable scope and a precise residual question: which measurement and control evidence genuinely represents the receiving configuration? The assigned owner will need to link the relevant reports and have their coverage assessed. Until that happens, the status remains a development comparison. This outcome is operational because it establishes the next work and who is accountable for it; it is not production approval disguised as form completion. The example data remain separate from the blank fields readers will use for their own sites.

Ref. GuideGxP — original operational method

Frameworks, scope and decision authority

Question	Source and category	Scope to verify	Site decision
Sterile process?	EU GMP Annex 1	Sterile manufacture; selected principles for non-sterile manufacture	Justify and document applicability and implementation.
Drug substance or product?	Part II and Annex 15	API framework; Annex 15 is optional supplementary guidance	Choose the framework before the qualification plan.
Ingredient or equipment?	21 CFR 210.3	US definition of component	Classify according to actual function and use.
Is USP <665> mandatory?	Informational compendial source	Verify whether the authority specifies otherwise	Do not infer mandatory status from the number or date.
Threshold proposed by Q3E?	ICH draft	No final requirement as of 10 October 2026	Separate future developments from adopted criteria.
What is the role of PIC/S?	Guidance and recommendations	Edition and implementation by the competent authority	Document adoption without implying EU amendments.

Ref. EU GMP Annex 1; EU GMP Annex 15; 21 CFR 210.3; USP <665> — public preview; ICH Q3E — EMA draft; PIC/S PI 006-4; GuideGxP — original operational method

Complete TL-001 and hand over the brief

Fields that make the brief reviewable

Field	Useful entry	Issue to keep visible
Product and stage	SB-M01: drug-substance development; fictional identity.	Do not turn a closed configuration into a sterility claim.
Boundaries and interfaces	Revision-controlled configuration, drawing and external owners.	The supplier document may not cover site integration.
Applicability	Source, version, jurisdiction, rationale and reviewer.	Drafts and informational references retain their status.
Decisions and approvals	Authorised function, name, date, scope and reference.	An unresolved gap needs an action and owner, not a generic signature.

Ref. GuideGxP — original operational method

When reviewing TL-001, GuideGxP suggests a cross-check: one person describes the path from the drawing and another checks whether the brief names the same boundaries. This editorial exercise is particularly useful for sampling and temporary connections, which are easily omitted from a description centred on the main bag. Each difference is recorded as a question to resolve, together with the expected document. There is no need to assume a favourable answer in order to complete the form; what must be made visible is that the decision still depends on that information.

Ref. GuideGxP — original operational method

Finally, retaining the rationale for exclusions helps the project to be reviewed when its use changes. If a previously external stage is integrated, the reviewer can identify the affected boundary and request a new assessment rather than automatically applying the old outcome. The closure reference should point to the decision resolving the specific issue and to the evidence examined. Attaching a received document is progress in documentation; declaring its relevance remains a separate act assigned to the competent reviewer.

Ref. GuideGxP — original operational method

Check before proceeding

Six answers to make verifiable

- Are the product, stage and state to be maintained defined without deductions based solely on single-use material?
- Does the boundary include inlets, outlets and branches, with consistent revision references?
- Is each source distinguished by authority, version and scope, with drafts and informational references recognisable?
- Do external interfaces have an owner and a governing document, even when excluded from the guide?
- Do the technical decision, quality judgement and regulatory assessment have assigned responsibilities and verifiable delegated authority?
- Does the handover to URS, risk analysis and supplier management preserve the open gaps and the next decision?

Ref. GuideGxP — original operational method

Part 01 / Chapter 02

URS and verifiable interfaces

Turn intended use into observable, verifiable requirements. Define how each requirement will be demonstrated and who manages each interface before approving the design.

Related tools TL-002, TL-001, TL-007, TL-009, TL-017

A requirement describes a function

A useful URS enables the designer and the verifier to answer the same question. “GMP-suitable system” expresses an intention but does not clarify which function must be demonstrated, under what conditions or with what evidence. EU GMP Annex 15 places user requirements, or the functional specification, at the start of the lifecycle and includes quality elements and GMP risks. Within its applicable scope, the URS becomes a reference for subsequent verification, rather than merely an attachment to a commercial enquiry.

Ref. EU GMP Annex 15

The process need should be distinguished from the proposed solution. The need may concern transferring a particular material while maintaining conditions established by the site; the solution may include a type of bag, a connection or a handling system. If the URS contains only product names, a technically different alternative becomes difficult to assess. If it contains only abstract needs, the supplier does not know which result to demonstrate. A requirement should bring together the function, relevant conditions and verification pathway, keeping what remains a design preference recognisable.

Ref. EU GMP Annex 15

Design qualification, DQ, compares the design with GMP and the approved URS within the relevant scope. A catalogue statement may support one element of the assessment but does not demonstrate site-specific integration. For example, a connection identified as compatible by name does not demonstrate that the planned manual sequence is feasible with the actual access, orientation and supports. DQ must allow the requirement to be traced to the configuration examined and the conclusion, distinguishing documented conformity from an assumption still awaiting a test.

Ref. EU GMP Annex 15

GuideGxP recommends leaving numerical criteria blank in the clean template until an authorised rationale defines their value, unit, scope and source. The presence of a cell to complete does not justify inventing a provisional value. The criterion may require development work or a site decision; in that case, the gap should be declared before verification is performed. Reading the result and only then selecting a threshold that makes it appear acceptable removes the ability of the test to answer the original question.

Ref. GuideGxP — original operational method

In TL-002, the requirement ID remains stable even when its revision changes. The recommended rewrite replaces “compatible with the process” with a description of the function, material handled, configuration, relevant conditions and planned verification. A number does not need to be inserted immediately into every sentence: the evidence that will enable a decision needs to be recognisable. If an essential condition is missing, the requirement remains incomplete and the process owner must provide it. This distinction prevents the technical writer from filling a knowledge gap with a commercial detail.

Ref. EU GMP Annex 15; GuideGxP — original operational method

Operating envelope and transient conditions

The operating envelope proposed by GuideGxP includes the volume range, liquid properties, contact conditions, loads, handling, transport, storage and relevant transients. Nominal volume alone does not describe expected behaviour: filling, operation and emptying may represent different configurations. Even a maximum catalogue value may refer to a condition different from that of the process. The comparison must therefore record the basis of the data and the associated conditions, without introducing a universal safety margin or turning the declared extreme into an authorised operating range.

Ref. GuideGxP — original operational method

Contact time and temperature should be linked to the fluid and stage, rather than collected as unrelated maxima. The designer needs to understand which combination will actually be used and which configuration supports it. A known property of a raw material does not necessarily describe a process solution; a condition stated for an isolated article does not automatically represent the integrated assembly. Where the site lacks the necessary data, the assumptions register should identify the origin of the uncertainty and who will provide the information, keeping the affected assessment open.

Ref. GuideGxP — original operational method

Transients deserve dedicated questions because normal operation may not represent them. Installing the path, starting a transfer, a shutdown and removal after use change the activities and interfaces involved. The operational recommendation is to describe these states with the same precision used for steady production: configuration, action, conditions and responsibilities. A statement about routine operation is not presumed to cover every manipulation. Comparison with the available evidence establishes which states are represented and which require further investigation.

Ref. GuideGxP — original operational method

To avoid ambiguous comparisons, TL-002 keeps the site need separate from the candidate’s declared capacity. If the two fields coincide only in part, the conclusion should identify the supported portion and the portion not demonstrated. Deleting the initial assumption and replacing it with what the supplier offers is not useful: that change may alter the process or purchasing decision. The process owner assesses the consequence, Engineering verifies feasibility and Quality addresses the conditions supporting product quality.

Ref. GuideGxP — original operational method

Mechanical, digital and human boundaries

The interface register is an implementation approach recommended by GuideGxP, not the name of a mandatory GMP document. It should make the fluid path, supports, utilities, instruments, control and data connections, operators and responsibilities visible. Its value is in locating points where performance depends on two suppliers, or on a supplier and the site. If the dossier ends at the connector and the requirement starts with the integrated process, an area without evidence may remain between them, even though both documents are formally complete.

Ref. GuideGxP — original operational method

Both sides of each boundary are described. At the connection between an assembly and its support, for example, verification needs to establish which configuration is installed and which support is used. At the utility connection, it identifies who provides the required conditions and where they are documented. Water, gases, cooling and supplies should not be developed here as independent projects: the register links them to their respective documents. Exclusion from the SUS supply does not remove the need for an answer from the interface owner.

Ref. GuideGxP — original operational method

The transition from measurement to control is also a boundary. TL-007 examines the chain from the sensor to the data and decision, while the URS identifies which function must be achieved and who verifies its integration. If the supplier checks only the sensor output and the site checks only a screen, the link between the two bodies of evidence may be missing. The register enables a coherent test of the relevant chain to be requested, with declared revisions, responsibilities and conditions, without presuming that two separate checks automatically demonstrate the whole.

Ref. GuideGxP — original operational method

Manual operations constitute another design interface. An instruction may require confirmation that the operator cannot observe from the intended position; a connection may be accessible only by changing the approved arrangement. The recommended method is to include the operator in reviewing the sequence and to record the condition requiring verification. The existence of a written procedure does not demonstrate that the configuration allows it to be performed. An unowned point should become an assigned action before the ambiguity is transferred to acceptance testing or production.

Ref. GuideGxP — original operational method

From requirement to test

An understandable verification chain links the requirement, method, configuration, criterion, evidence and reviewer. The method may be a document comparison or a test at the appropriate location; the choice must address the function to be demonstrated. TL-002 offers DQ, FAT, SAT, IQ, OQ, PQ and another justified verification. The labels organise the pathway but do not make the evidence interchangeable. A test performed at the supplier remains useful only if its conditions and responsibilities allow the site to assess its relevance to the site's own conclusion.

Ref. EU GMP Annex 15

The site criterion should be established in the context of the configuration examined. GuideGxP recommends recording its source and rationale, as well as its value where numerical. A "compliant" box without a reference to the criterion does not allow the reviewer to reconstruct what was compared. If the requirement concerns a qualitative function, the observation or document demonstrating it needs to be described. Leaving a numerical field blank when the criterion is qualitative is correct; leaving the decision rule undefined is not.

Ref. GuideGxP — original operational method

The revision of the bill of materials, or BOM, forms part of the configuration identity. If DQ assessed one assembly and the test uses another, the result cannot be attributed to the original design without assessing the difference. The link with TL-009 helps keep the drawing, contact path and components consistent. TL-017, in turn, organises the qualification evidence plan. The URS remains the reference for the question: the other tools develop the verification without replacing it with a collection of certificates that have not been related to the requirements.

Ref. EU GMP Annex 15; GuideGxP — original operational method

The review should distinguish test execution from requirement closure. A test may be finished but not assessable, for example because the configuration revision is missing or the condition used is not the one required. GuideGxP recommends recording the available result and the reason the conclusion remains pending. The action owner identifies the evidence to retrieve or the verification to repeat; the reviewer then assesses whether the gap has been resolved. Completion of the schedule is not the criterion for technical closure.

Ref. EU GMP Annex 15; GuideGxP — original operational method

Decisions before purchase

Before purchase, the URS allows essential requirements, preferences and unconfirmed assumptions to be separated. GuideGxP recommends keeping these distinctions explicit in clarification requests. A candidate may be interesting but not yet assessable for a necessary function; the useful response is to request evidence or define the development activity's scope, rather than grant implicit acceptance. The comparison retains its link to TL-001 so that a commercial proposal does not silently change the approved product, stage or boundary. Any changes return to the functions that defined the need.

Ref. GuideGxP — original operational method

ASTM E3051-25 is the current public reference for the scope of single-use system specification, design, verification and application. This identifies the edition and subject of the standard; it does not reconstruct proprietary clauses. Similarly, ASME lists BPE-2026, but the linked public contents page examined is a 2024 preview. A project adopting a standard must declare the edition actually used and access the relevant text. A catalogue or contents page replaces neither that access nor demonstration of the specific requirement.

Ref. ASTM E3051-25 — public scope; ASME BPE-2026 — publisher catalogue

Revision control preserves the reason for the choice. If a requirement changes because the intended use has changed, the affected verification needs to be reassessed. If only the solution changes, it is necessary to understand whether the new configuration continues to meet the requirement. These are different questions, even when they produce the same drawing update. In the proposed pathway, the revision records the origin, rationale, affected elements and competent authority. An old conclusion is not deleted: it is linked to the version to which it referred, making clear why it cannot automatically be extended to the new one.

Ref. EU GMP Annex 15; GuideGxP — original operational method

The transition to execution is defensible when the requirements to be verified, criteria and responsible people are recognisable, and an agreed approach exists for residual issues. This does not mean every study must already be complete at the quotation stage. It means the project does not hide an essential point within a commercial assumption. If a process condition is missing, its owner defines it; if candidate evidence is missing, the supplier clarifies coverage; if the criterion is missing, the authorised function establishes its basis before the test intended to support the conclusion.

Ref. EU GMP Annex 15; GuideGxP — original operational method

Worked case

Illustrative case From a "200 L" request to a verifiable URS

Illustrative example with fictional identities and data. Selvara Biologics prepares the URS to compare configurations for programme SB-M01, concerning development of a monoclonal antibody drug substance. The reference configuration is SU-ASM-UP-01, revision A. A seed working volume of 20 L, a production bioreactor working volume of 200 L and a separately measured harvest pool of 180 L are declared. The decision concerns which evidence to request from candidates and how to verify their integration, not authorisation of an already qualified manufacturing process.

Engineering starts from TL-001 rather than simply writing "200 L single-use bioreactor". It keeps the capacity required for the production stage separate from the seed conditions and the harvest data. The conditions field describes the process to be represented, while the site still needs to justify the performance criterion. No complete balance linking the volumes is available; a harvest yield is therefore not introduced. Even a proposal stating the same working volume will need to be compared under the relevant measurement and control conditions.

The interface register includes gas supply and exhaust, cooling and temperature, electrical power and controls, upstream preparation and downstream transfer. For each item, Engineering requests the reference for the site portion and the supplied portion. The question to the supplier becomes concrete: which evidence represents this connection in the candidate configuration? If the document ends at the supply boundary, the plan identifies the integration verification still required. Flow rates, power ratings or utility performance are not invented to fill the fields that remain open.

The process owner must provide the conditions that make capacities comparable. The qualification reviewer can then associate each requirement with a verification method, location and configuration. Numerical criteria are not present in the case data: they therefore remain blank in the operational template, with an assigned action. Choosing an entry such as DQ or OQ organises the work but does not anticipate its result. TL-007 receives questions about the measurement chain; TL-009 maintains the identity of the contact path and its revisions.

Design review must also check that the assessed bill of materials matches the one to which the evidence refers. The case provides neither complete reports nor confirmation at the receiving scale. These omissions are described as gaps to close, rather than as already demonstrated defects in the candidate. The comparison can continue to identify the necessary information and plan verification. The suitability decision remains pending wherever coverage is not demonstrated; the team does not alter the criterion after seeing favourable performance.

The operational outcome is a URS that preserves the original need and makes the pathway to testing explicit. Engineering is responsible for interface consistency; the process owner defines the conditions; Quality and qualification functions govern criteria and authorisations according to the site's assignments. TL-017 will bring together the evidence plan, but the requirement will remain traceable in TL-002. The residual issue is whether candidate data represent the receiving scale: only a review of relevant evidence can support the conclusion, without turning this example into an approved protocol.

Ref. GuideGxP — original operational method

Interfaces and tests

Interface	Requirement to clarify	Relevant test	Owner and evidence
Fluid path–support	Configuration installable according to the intended use.	Design comparison and configuration verification.	Engineering; revision-controlled drawing and bill of materials.
Gas and temperature	Conditions required by the process and supply boundaries.	Evidence of the connection under the defined conditions.	Process owner and utility owner; site references.
Sensor–control	Function of the measurement chain and use of the data.	Verification of the relevant path, not just its individual endpoints.	Automation and measurement owner; TL-007.
Operator–instruction	Sequence feasible in the planned arrangement.	Review of the manipulation and confirmation signals.	Production; controlled configuration and instruction.
URS–DQ	Design meeting the approved requirements.	Rationale, gaps and verification references.	Engineering and Quality; current URS and DQ record.

Ref. EU GMP Annex 15; GuideGxP — original operational method