Raman spectroscopy in GMP environments

Learn how Raman spectroscopy systems are deployed in good manufacturing practices (GMP)-regulated pharmaceutical and biopharmaceutical manufacturing environments. This article provides an overview of qualification and validation principles, software and data-integrity requirements, supplier and user responsibilities, and industry and regulatory frameworks.

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Why Raman system installation in GMP environments deserves specific guidance

Raman spectroscopy is increasingly used in pharmaceutical and biopharmaceutical manufacturing because it can provide real-time, in-line, or in-situ information about process state without relying solely on offline sampling. In upstream bioprocessing, Raman spectroscopy can support process understanding, feed strategy decisions, and scale-up by creating a continuous spectral view of the bioreactor. In other regulated applications, Raman spectroscopy may support raw material verification, process monitoring, or analytical workflows where data must be reliable, traceable, and available for review.

This is precisely why installation in a good manufacturing practice (GMP) environment requires more than a conventional instrument installation checklist. The key question is not only whether the analyzer, probe, fiber-optic cables, and software are installed correctly. It is whether the complete measurement system is fit for its intended use, whether the generated data can be trusted, and whether responsibilities are clearly defined between the supplier, system integrator and regulated user.

The practical challenge is that GMP is often discussed in a very generic way. Users may hear terms such as IQ, OQ, PQ, Part 11, Annex 11, validation, qualification, data integrity, GAMP, ASTM E2500, and USP <1058>, but still be unsure what these mean for a Raman process analytical technology (PAT) system. This article is intended to close that gap. It explains what is at stake, what usually brings a Raman installation into GMP scope, which frameworks may be relevant, and which documentation can normally be expected from the Raman analyzer supplier versus what must be defined and approved by the pharmaceutical manufacturer.

The most important point is also the simplest: GMP compliance is not a label attached to an analyzer. It is the outcome of a documented, risk-based implementation within a defined process, facility, and quality system.

When does a Raman installation fall under GMP requirements?

A Raman system does not automatically fall under GMP requirements simply because it is installed in a pharmaceutical facility. GMP applicability is driven by intended use. If Raman measurements influence process control, batch decisions, product quality assessment, release strategy, process validation, or regulatory submissions, the system is likely to fall within the regulated scope of the pharmaceutical quality system.

This distinction is essential for both suppliers and users. Two identical Raman analyzers can have different compliance expectations depending on how they are used. One analyzer may support development scientists in a laboratory where the data are exploratory. Another analyzer may be connected to a GMP reactor, transfer spectral data to a PAT platform, and provide model outputs that are reviewed by operations, manufacturing science and technology (MSAT), or quality teams. The hardware may be very similar, but the compliance context is different because the intended use, data flow, and product-quality impact are different.

For Raman spectroscopy, the regulatory relevance often increases when the system is part of a broader PAT strategy. PAT applications are designed to improve process understanding and control through timely measurements of critical process and quality attributes (CPP and CQA). When Raman data are used in this way, the installation should be considered not only as analytical equipment but as part of a process monitoring, data management, and decision-support system.

The first question in a GMP Raman system installation project should therefore not be “is this instrument GMP compliant?” but questions such as:

- What is the intended use of the Raman system?
- What decisions will be made from its data?
- What risks could arise if the measurement, model or data record is incorrect, unavailable or unreliable?

Which GMP and validation frameworks matter for Raman spectroscopy?

There is no single Raman-specific GMP installation standard. Instead, Raman projects are typically evaluated through a combination of regulatory requirements, guidance documents, company procedures and risk-based validation frameworks. The applicable framework depends on geography, product type, process criticality, system architecture and intended use.

In the United States, regulations and guidance from the Food and Drug Administration (FDA) may be relevant, including 21 CFR Parts 210 and 211 for drug manufacturing, 21 CFR Part 11 when electronic records or electronic signatures are used, and the FDA PAT guidance for innovative pharmaceutical development, manufacturing, and quality assurance. In Europe, EU GMP Annex 15 is directly relevant to qualification and validation, while Annex 11 is relevant when computerized systems are used in GMP activities. For international organizations, PIC/S guidance and local regulations may also need to be considered.

Industry frameworks then help translate regulatory expectations into workable project approaches.

- ASTM E2500 – provides a science- and risk-based approach for specification, design and verification of pharmaceutical and biopharmaceutical manufacturing systems.
- ICH Q10 – describes the pharmaceutical quality system framework that supports lifecycle management, change control, continual improvement, and maintenance of the validated state throughout commercial operation.
- ICH Q14 – provides guidance for analytical procedure development and lifecycle management, including science- and risk-based approaches relevant to PAT methods and chemometric model development.
- ISPE GAMP 5 – is widely used for computerized systems validation and lifecycle management.
- USP <1058> – is often used for analytical instrument qualification and provides language around fitness for intended use.

These frameworks are complementary rather than mutually exclusive. A Raman installation may involve all three of these elements:

- instrument qualification
- manufacturing-system verification
- software lifecycle validation

The user's own quality system remains the deciding layer. A global pharmaceutical company may have site-specific validation master plans, SOPs, risk assessment templates, data-integrity standards, and supplier qualification processes. A supplier can provide documentation and technical evidence, but the regulated user must determine which framework applies and how it is implemented locally.

Which frameworks are commonly encountered in GMP Raman spectroscopy projects?

Industry frameworks, pharmacopoeial chapters, and analytical lifecycle guidance documents help translate regulatory expectations into workable implementation approaches for PAT and Raman spectroscopy applications (see table below).

Framework	Primary focus	Typical relevance to Raman spectroscopy
FDA PAT guidance	Positions real-time process understanding and quality assurance as part of modern pharmaceutical manufacturing	Why Raman is often discussed as a PAT technology rather than only as an analytical instrument
21 CFR Part 11	Relevant when electronic records and electronic signatures are used for FDA-regulated activities	Use carefully; software can support Part 11 controls, but the user must implement procedures and governance
EU GMP Annex 11	Relevant to computerized systems used in GMP activities, including lifecycle validation, risk management, supplier oversight, and data integrity	Useful for the supplier/user responsibility discussion because the regulated user remains accountable
EU GMP Annex 15	Defines principles for qualification and validation of facilities, equipment, utilities, and processes	Use to explain URS, DQ, IQ, OQ, PQ, VMP, change control, and lifecycle thinking
ASTM E2500	Provides a science- and risk-based approach to specification, design, and verification of pharmaceutical systems	Use to support a practical, risk-based tone, not a paperwork-driven tone
USP <1058>	Provides a framework for establishing fitness for intended use of analytical instruments and systems	Useful when users view a Raman analyzer as an analytical instrument with qualification expectations
ISPE GAMP 5	Widely used for computerized systems validation and lifecycle management	Use for software/data-management aspects, especially when Raman technology connects to PAT or automation platforms
ICH Q10	Pharmaceutical quality systems and lifecycle management	Particularly relevant when a Raman system is used as a PAT method and when chemometric model development, validation, and lifecycle management are part of the implementation
ICH Q14	Analytical procedure development and lifecycle management	Useful for explaining change control, periodic review, continual verification, CAPA processes, and maintenance of the validated state after implementation
USP <1037> Process Analytical Technology – Theory and Practice	Application of PAT within pharmaceutical manufacturing	Provides practical context for implementation of Raman spectroscopy and other PAT tools within pharmaceutical development and manufacturing environments
Ph. Eur. 5.25 Process Analytical Technology	European pharmacopoeial framework for PAT approaches	Relevant for understanding deployment of Raman spectroscopy within PAT-based monitoring and control strategies in regulated environments
BioPhorum PAT Roadmap	Industry best practices for PAT adoption and scale-up	Useful for explaining organizational, technical, and lifecycle considerations that influence successful PAT deployment
BioPhorum PAT Interoperability & Scalability Guidance	Integration and lifecycle management of PAT systems across sites and scales	Particularly relevant when Raman data must interact with PAT platforms, historians, automation systems, and digital manufacturing environments

What makes Raman spectroscopy different from conventional analytical instrumentation?

Understanding the full validation scope

Raman spectroscopy can look familiar to validation teams because it is an analytical technology. Yet, like many process spectroscopy PAT installations, a Raman implementation often involves a broader qualification and validation scope than a conventional laboratory instrument. The measurement chain normally includes the analyzer, optical components, Raman probes, fiber-optic routing, process interface, software, calibration routines, model files, data transfer, user access controls, and sometimes links to automation or data platforms. In GMP applications, the validation scope may therefore extend beyond the instrument body.

When data processing becomes part of GMP compliance

A second difference is the role of spectral data processing and interpretation. In many Raman applications, the business value does not come directly from the raw spectrum itself, but from how spectral information is transformed into actionable process information. This may involve simple data-processing steps such as baseline correction, normalization, peak-area calculations, or spectral comparisons, as well as more advanced chemometric or predictive models. For example, in biopharmaceutical manufacturing, Raman technology is often used to derive information such as glucose and lactate concentrations, viable cell density, metabolite trends, process-state indicators, or other critical process attributes. The primary value lies in these derived insights rather than in visual inspection of the spectrum alone.

When the derived information is used in a GMP context, the data-processing approach becomes part of the compliance discussion. Validation considerations may therefore extend beyond the analyzer hardware to include the intended use of the analysis method, spectral preprocessing, model, or algorithm version control where applicable, acceptance criteria, change management, and ongoing performance monitoring.

Continuous monitoring and data integrity considerations

A third difference is that Raman systems may operate continuously. Continuous data generation changes the way teams think about data integrity, review, storage, and trend analysis. It also raises practical questions about what constitutes the GMP record, which software is the system of record, how data are archived, who can modify configuration settings, and how deviations are handled when communication or data transfer fails.

This does not make Raman spectroscopy unsuitable for GMP environments. On the contrary, it explains why a clear, risk-based and responsibility-aware implementation approach is so important.

How does GMP implementation differ for single-use bioprocessing?

Single-use technologies are now widely used in pharmaceutical and biopharmaceutical manufacturing, particularly during process development, scale-up, and commercial biologics production. The increasing adoption of single-use bioreactors has raised new questions around Raman system qualification, validation, and lifecycle management in GMP environments. Raman spectroscopy is frequently integrated into single-use bioreactor platforms through dedicated optical interfaces designed to enable real-time monitoring without compromising sterility.

A key benefit of single-use technologies is that certain activities traditionally performed by the manufacturer, such as cleaning validation and aspects of sterilization qualification, are reduced or transferred to qualified suppliers. This can simplify implementation, reduce validation effort, shorten deployment timelines, and lower contamination risks when compared with conventional reusable systems.

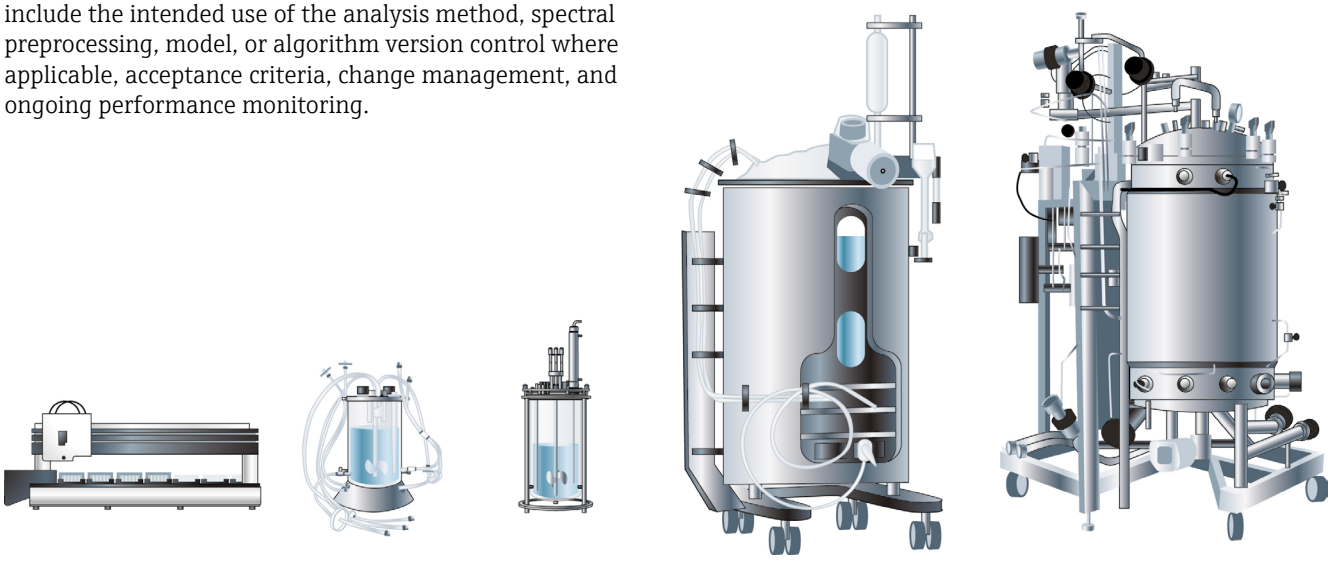

Figure 1: Raman spectroscopy can be integrated into stainless-steel or single-use bioprocessing environments when the complete measurement solution is qualified for its intended use.

However, single-use technology does not eliminate GMP responsibilities. Instead, it changes where some of those responsibilities reside. The regulated user remains responsible for confirming that supplied components are suitable for their intended use, maintaining appropriate supplier oversight, and ensuring that applicable documentation is available within the overall GMP documentation package.

For Raman installations, qualification and validation activities should consider the complete measurement chain, including the analyzer, probe, optical interface, software, data flows, and any associated chemometric models. Additional considerations may include supplier-provided material certifications, certificates of conformity, sterilization-related documentation, extractables and leachables assessments where applicable, and management of component changes throughout the lifecycle.

The fundamental GMP principles therefore remain unchanged. Intended use, risk assessment, qualification, validation, data integrity, change control, and lifecycle management remain necessary regardless of whether the Raman system is deployed in a stainless-steel or single-use process platform. The primary difference is that single-use technologies can reduce certain validation burdens while increasing the importance of supplier qualification and supplier documentation.

Who is responsible for GMP compliance in a Raman system installation?

GMP compliance is achieved through the complete implementation—not through the instrument alone.

Supplier
- Provides equipment
- Provides documentation
- Provides qualification support

Regulated user
- Defines intended use
- Approves validation strategy
- Maintains validated state

No supplier can make a pharmaceutical installation GMP compliant simply by declaration. A supplier can provide a GMP-ready platform, documented design controls, product documentation, qualification support, and technical evidence. The supplier can also provide trained service personnel and project-specific support. However, the regulated user remains responsible for demonstrating that the complete system is fit for its intended use within the user's process and quality system.

This point is often the greatest source of project misunderstanding. Users may ask whether the analyzer is GMP certified, whether supplier IQ/OQ documentation is sufficient, or whether a Part 11-capable software package automatically makes the overall installation compliant. These questions are understandable, but they reflect a misconception. GMP compliance is not a single vendor certificate. It is a documented state of control across equipment, software, procedures, people, data, and process use.

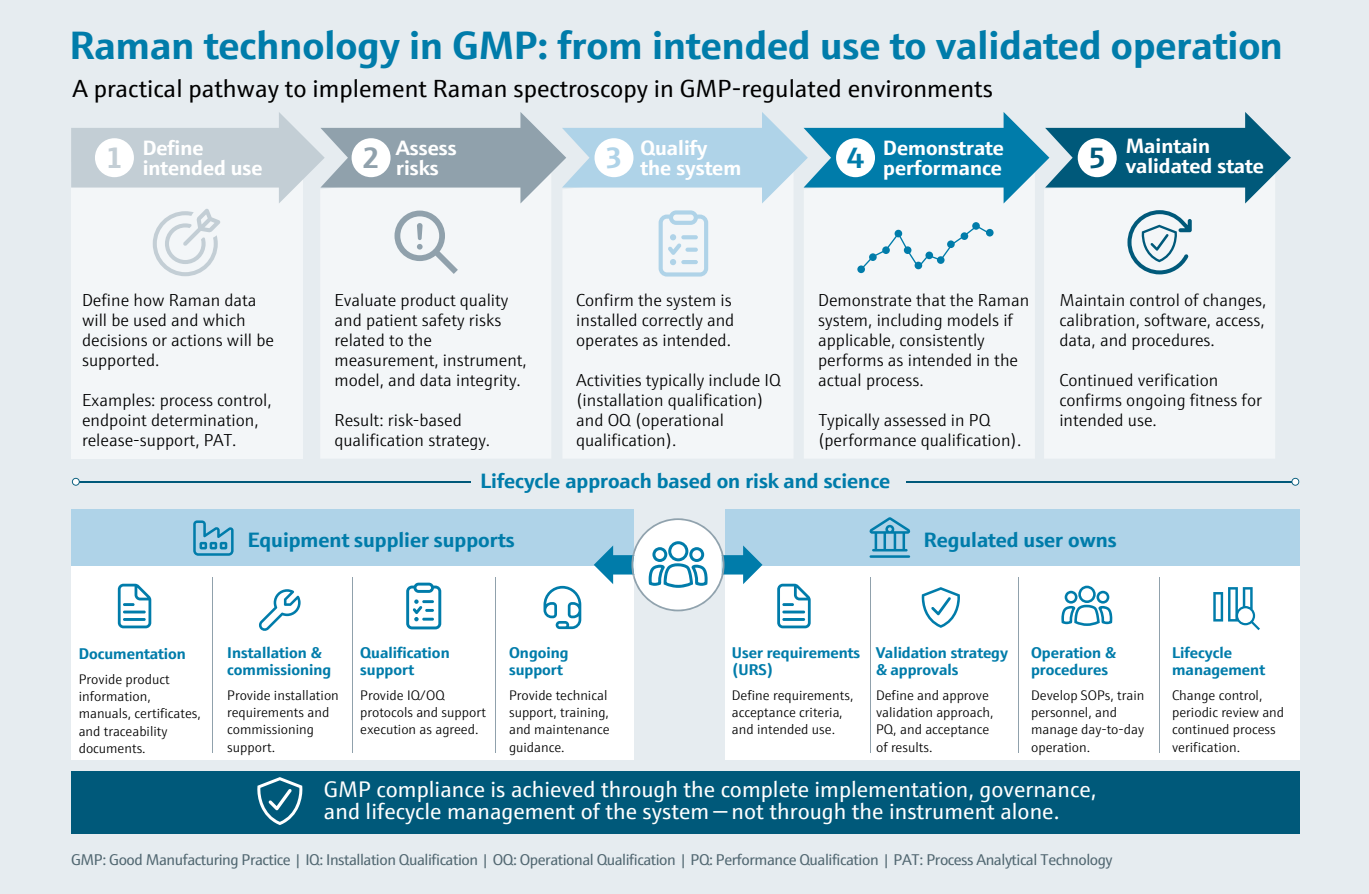

Figure 2: GMP implementation pathway for Raman spectroscopy, from intended use and risk assessment through qualification, validation support, and lifecycle management.

Supplier responsibilities

The supplier is responsible for the design, performance, and documentation of the Raman system it provides. This typically includes product specifications, installation requirements, operating limits, calibration information, software documentation, and maintenance guidance. Depending on the supplier and project scope, qualification-support documentation such as IQ/OQ packages, requalification protocols, or electronic record/electronic signature assessments may also be available.

User responsibilities

The regulated user remains responsible for defining the intended use of the Raman system and determining how the generated data will be used within the manufacturing process. This includes approving requirements, assessing product-quality risks, defining procedures, training personnel, managing access controls, approving deviations, and maintaining the validated state throughout the system lifecycle.

How qualification typically works for Raman systems

Qualification should be proportionate to the intended use and system risk. A Raman system used for non-GMP development work may not need the same documentation burden as a Raman system used to support GMP process control. In a regulated installation, however, qualification usually follows a lifecycle logic that connects requirements, risk, design, installation, operation, performance, and ongoing control.

The starting point is the user requirements specification (URS). The URS should describe what the user needs the Raman system to do, which functions are GMP relevant, which interfaces matter, what data must be retained, who needs access, and which performance expectations must be demonstrated. Vendor documentation can support this work, but the URS should be owned, reviewed, and approved by the user.

Risk assessment then determines how much qualification effort is justified. For example, a function that merely displays a trend for process-state awareness may have a different validation criticality than a model output used to adjust feed rate in a GMP process. A data-transfer interface used to create GMP records may require more attention than a non-critical export function used for exploratory analysis. This risk-based approach keeps the validation effort focused on patient safety, product quality, and data integrity rather than on low-value testing.

The difference between IQ, OQ, and PQ

- **Installation qualification (IQ)** – verifies that the delivered system is present, correctly installed and suitable for its operating environment. This may include verification of analyzer identity, probe and fiber routing, software version, key configuration settings, environmental conditions, utilities, calibration status, and relevant documentation. The supplier can provide installation requirements and IQ documentation and may help execute or support these activities. The user must approve the protocol, assess deviations, and retain the qualification evidence within its quality system.
- **Operational qualification (OQ)** – verifies that the system functions as expected. For a Raman system, this may include basic instrument operation, laser enablement controls, spectral acquisition, probe channel selection, user access, audit-trail behavior, data transfer, model loading, alarm or diagnostic functions where applicable, and report or export functions. Again, supplier protocols can be valuable, but they should be reviewed against the user's intended use and site procedures.
- **Performance qualification (PQ)** – demonstrates that the system performs reliably for the actual process, product and application. This is where Raman spectroscopy becomes strongly application-specific. The supplier may support measurement strategy, application development or troubleshooting, but the pharmaceutical manufacturer must approve the process-specific evidence. PQ may include confirmation that measurement performance, model outputs, sampling alignment, operating range, and data review approach are suitable under real or representative manufacturing conditions.

Qualification does not end at go-live. A GMP Raman system must remain in a controlled state. Changes to software, model files, probe configuration, calibration routines, network interfaces, operating procedures, or intended use should be assessed through change control. Periodic review, preventive maintenance, recalibration, or requalification may be needed depending on the user's procedures and risk assessment.

What documentation is typically provided by equipment suppliers?

The answer should be clear to this practical customer question: what will the manufacturer provide, and what must we still do ourselves? As a general approach, equipment suppliers typically provide the documentation needed to understand, install, operate, and maintain a Raman system. Depending on the supplier, application, and project scope, additional validation-support documentation may also be available.

For Raman data-management and software-related offerings, available support may include IQ/OQ or re-OQ documentation, Part 11 questionnaires, electronic record/electronic signature assessments, and other validation-support documents. These should be positioned as support for the customer's qualification and validation work, not as a substitute for the customer's GMP approval. Where a document is not part of the standard delivery, the page should clearly state that it may be available on request, subject to product configuration and project scope.

Understanding the boundaries of supplier support

While equipment suppliers can provide documentation, technical expertise, and qualification support, regulatory responsibility for GMP compliance remains with the pharmaceutical manufacturer. Suppliers can help users understand system capabilities, installation requirements and available qualification documentation, but they do not determine how the measurement system will be used within a specific manufacturing process.

Activities such as defining intended use, approving validation strategies, managing change control, establishing operating procedures, and maintaining the validated state remain the responsibility of the regulated user. This distinction is fundamental to GMP implementation and applies regardless of the specific technology or supplier involved.

Understanding these boundaries early in a project helps establish realistic documentation expectations and supports a more efficient qualification and validation process.

Data integrity, software and electronic records

Data integrity is central to any GMP Raman installation because Raman systems generate digital records. These may include raw spectra, processed spectra, model outputs, diagnostic data, audit trails, configuration records, reports, and exported files. If these records are relied upon for GMP activities, the user must be able to demonstrate that they are attributable, legible, contemporaneous, original or true copy, accurate, complete, consistent, enduring, and available according to applicable procedures.

Software capability is necessary but not sufficient. A Raman software platform may support user management, permissions, audit trails, data storage, data transfer, and electronic-record workflows. Those capabilities help the user build a compliant implementation. However, the user must configure and operate them correctly. User accounts, access levels, password rules, backup strategy, archive strategy, periodic review, SOPs, and training are all controlled within the user's quality system.

Interfaces require particular attention. When Raman outputs are sent to a DCS, SCADA, LIMS, historian or PAT platform, the validation scope should define which system is the system of record, which data must be retained, whether transfer is automatic or manual, how failures are detected, and how records are reconciled. If Raman results are used to trigger process actions, the risk assessment should consider both measurement reliability and data-transfer reliability.

Common misconceptions

"The Raman analyzer is GMP certified."
A more accurate statement is that the analyzer can be supplied with documentation and features that support use in GMP-regulated environments. GMP compliance depends on how the complete system is implemented and controlled by the user.

"IQ/OQ makes the process validated."
IQ/OQ can demonstrate that a system has been installed and operates according to predefined requirements. It does not by itself demonstrate that the system performs for a specific manufacturing process, product, model, and control strategy. That is the purpose of PQ and ongoing verification.

"Part 11 equals GMP compliance."
Part 11 addresses electronic records and electronic signatures. GMP compliance is broader and includes quality systems, procedures, training, qualification, validation, change control, deviations, data integrity, and continuous control.

"The supplier owns the URS."
The supplier may provide templates, technical input or review comments, but the URS should reflect the user's process, intended use and quality requirements. The regulated user should approve and own it.

"A model transferred from development is not automatically valid to manufacturing."
Model transfer may be possible and valuable, but suitability must be demonstrated for the intended manufacturing use. Scale, matrix, process conditions, sampling strategy, and control relevance must be considered.

Glossary

Term	Plain-language explanation
Audit trail	A secure, time-stamped record of user actions and system events relevant to data and configuration.
cGMP	Current good manufacturing practice: commonly used in the United States to emphasize current regulatory expectations.
Chemometric model	A mathematical model that converts spectral information into process-relevant outputs.
Data integrity	The completeness, consistency and trustworthiness of data throughout its lifecycle.
Electronic record / electronic signature	Digital records and signatures that may need to meet regulatory controls such as 21 CFR Part 11.
GMP	Good manufacturing practice: requirements for consistent production and control of medicinal products according to quality standards.
GxP	A collective term for regulated good practices, including good manufacturing practice (GMP), good laboratory practice (GLP), good clinical practice (GCP), and good distribution practice (GDP).
IQ	Installation qualification: documented verification that the system is installed correctly.
OQ	Operational qualification: documented verification that the system operates as intended.
PAT	Process analytical technology: a framework for timely measurement and control of manufacturing processes.
PQ	Performance qualification: documented evidence that the system performs for the actual process and intended use.
URS	User requirements specification; the user-owned document that defines what the system must do for its intended use.
Validated state	The controlled condition in which the system continues to meet approved requirements and intended use.

FAQ

Is Raman spectroscopy suitable for GMP?
Yes. Raman spectroscopy is widely used in pharmaceutical and biopharmaceutical manufacturing to support process monitoring, PAT initiatives, and process understanding. Qualification and validation requirements depend on intended use.

Is IQ/OQ always required for Raman system operations?
Not always. The need and extent of IQ/OQ depend on intended use, process criticality, site procedures, and regulatory context. In regulated manufacturing, IQ/OQ is commonly expected.

Can Endress+Hauser provide IQ/OQ documentation?
For relevant Raman configurations and software offerings, IQ/OQ or re-OQ support documentation may be available, subject to product version, configuration, and ordered scope.

Who owns PQ?
The pharmaceutical manufacturer owns PQ because PQ must demonstrate performance in the actual process, product, and quality system.

Does Part 11 capability make the installation compliant?
No. Part 11-capable functionality supports compliance, but configuration, procedures, user management, record review, and data governance remain user responsibilities.

Does a Raman model need validation?
If a model output is used for GMP decisions, the model lifecycle should be addressed in the validation strategy, including intended use, acceptance criteria, change control, and ongoing monitoring.

Can development models be transferred to GMP manufacturing?
Potentially, but transferability must be justified and demonstrated for the intended manufacturing use.

What is the most important first step?
Define intended use. Without a clear intended use, the validation scope, documentation needs, and responsibility split cannot be correctly defined.

Do single-use bioreactor installations require a different GMP approach?
The fundamental GMP principles remain the same. The intended use, qualification strategy, validation approach, and data-integrity requirements are comparable to those of traditional stainless-steel installations. However, additional attention is often given to disposable components, supplier documentation, change control, and verification that single-use process interfaces remain suitable for their intended use throughout the manufacturing lifecycle.

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