

This article focuses on construction contractors who can deliver qualified facilities and presents the advantages of using a construction contractor who can perform Commissioning and Qualification.

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A Practical Guide to Construction, Commissioning and Qualification Documentation – and its Critical Role in Achieving Compliance

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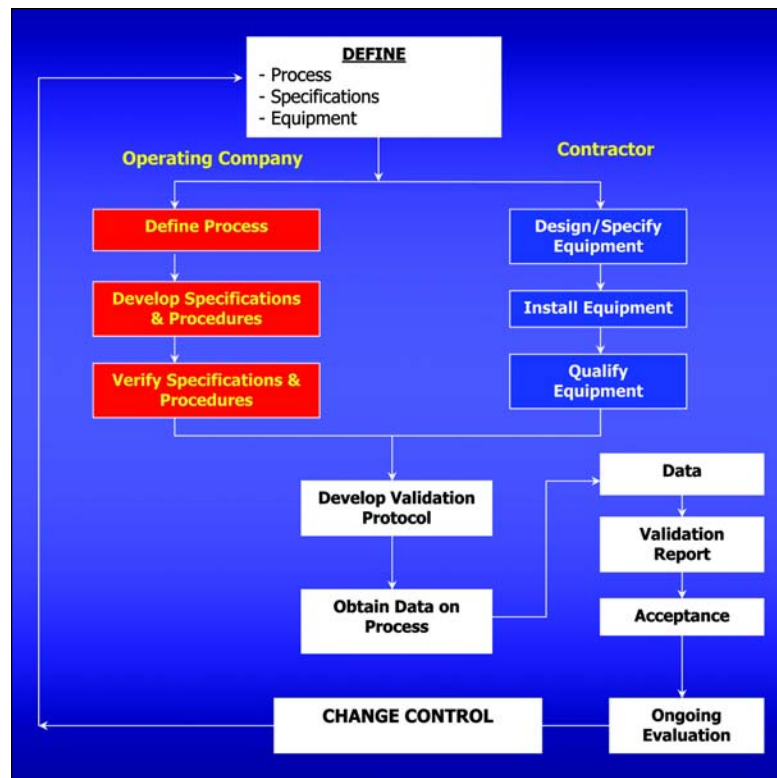
Good documentation is essential for pharmaceutical and biotech manufacturing facilities to achieve regulatory compliance. As defined by the Food and Drug Administration (FDA), “Validation is a *documented* program providing a high degree of assurance that a process/system consistently meets pre-determined specifications.” The clear presumption is that if the required activities have not been properly documented, then they have not been performed.

Naturally, the initial focus must be on the proper construction and start-up of the facility. Yet, a well-constructed facility that is on time, within budget, and whose every system is performing to specifications is of no value to the operating company if the associated documentation does not effectively support the qualification process – it is a classic case of failing to see the forest through trees. In fact, the construction contractor must appreciate the significance of documentation, and make it an

integral part of the construction planning, implementation, and commissioning process from day one.

Note: the term “Construction Contractor” is used to indicate a third party company responsible for construction, commissioning and qualification. This article focuses on construction contractors who can deliver qualified facilities. It also presents the advantages of using a construction contractor who can perform C&Q, as well as construction led rather than design led projects. A “full service provider” could provide all of these activities. These activities could be provided in

Figure 1. Validation life cycle.



Commissioning and Qualification

part by a Construction Management (CM) contractor, a commissioning contractor, a qualification contractor and the operating company.

Turn Over Package (TOP): Laying the Foundation

Good documentation is an essential part of the Quality Assurance (QA) system. For new and renovated facilities, Commissioning and Qualification (C&Q) are key aspects of cost and schedule. Therefore, documentation – in the form of the TOP, C&Q protocols, and other required documents – plays a pivotal role in ensuring a compliant facility. Every operating company has specific standards and methodologies for C&Q. The construction contractor's job is to make sure that the TOP enables the operating company to effectively carry out its QA strategy. Therefore, the TOP must be well-organized, meet the operating company's expectations, and provide the proper level of documentation quality.

To be successful, an integrated documentation process must start very early in the project in conjunction with the planning of C&Q. It must involve engineering, construction, and qualification/validation. Moreover, project documentation requirements, and the roles and responsibilities for the operating company, construction contractors, and vendors alike, must be clearly defined.

Too often, documentation work is delayed until the later

stages of the project, or the effort required to do it successfully is underestimated. For example, on an 18-month project, the QA/documentation officer should be involved by the first quarter of the project – during the planning phase – to begin to organize the TOP to meet the operating company's needs and expectations. It is well worth the small investment to bring that individual on board early to avoid problems during the qualification process, and ultimately, reduce time to market. This approach eliminates duplication of effort by leveraging documentation from commissioning into Installation Qualification (IQ). IQ is approximately 30% of the qualification effort; by leveraging commissioning documentation, a savings of approximately 50% of IQ effort could be made, resulting in an overall saving of 15% of qualification time.

The Validation Life Cycle

Just as good documentation is required to achieve regulatory compliance, clear user specifications that are fully understood by the construction contractor are required to meet the operating company's unique needs and expectations. If the constructor fails to understand these from the outset, the TOP is likely to be inadequate. Therefore, for every step taken by the operating company, engineers and construction contractor, a high level of integration is required to ensure that the resulting documentation is appropriate, compliant, and structured in a meaningful manner - *Figure 1*. The diagram

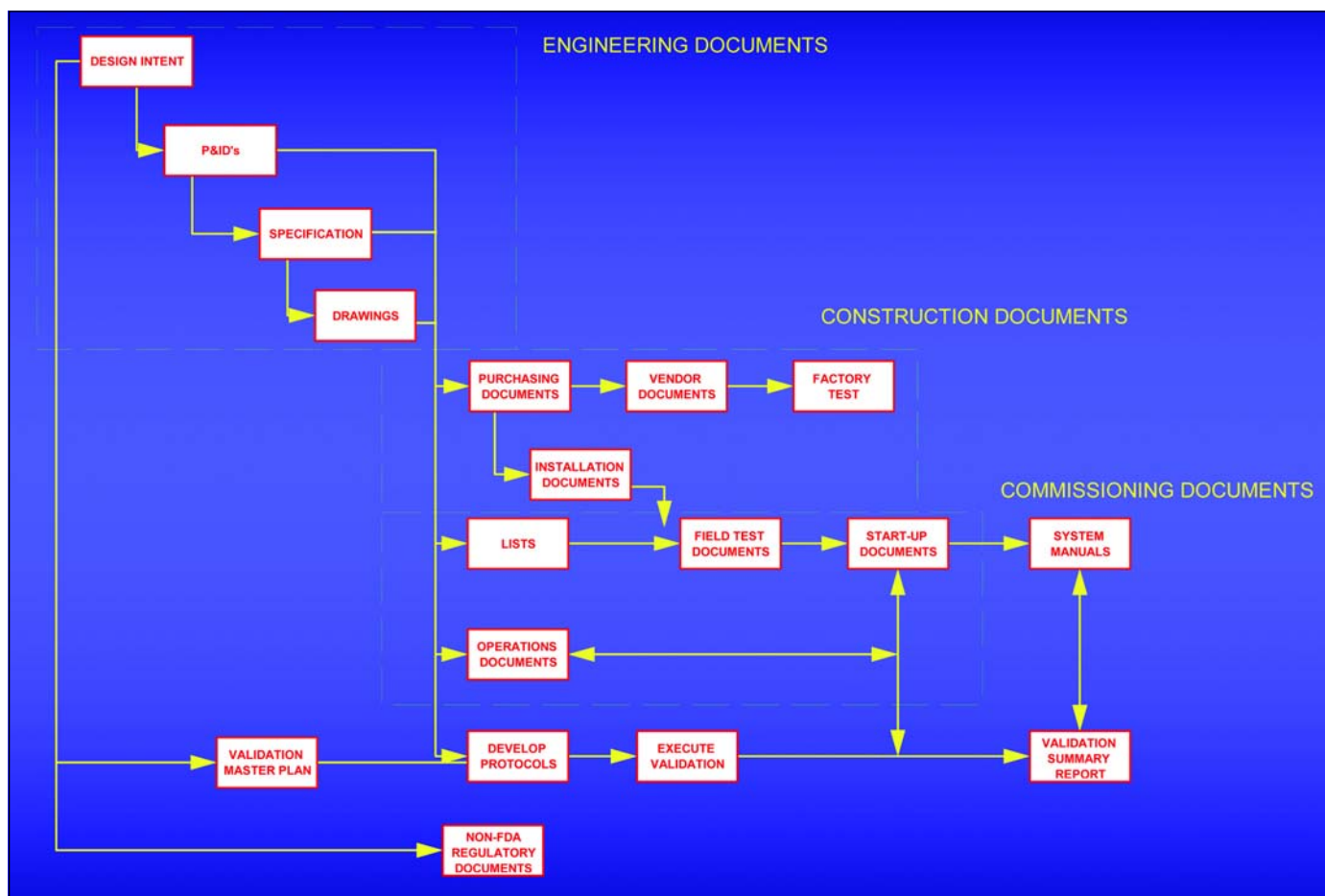


Figure 2. Document hierarchy.

illustrates the importance of the “definition” stage for both the operating company and the contractor. In all aspects of the life cycle, documentation/data is a very critical element.

The operating company’s definitions of specifications and process requirements drive the whole project. Specifically, the operating company defines the process, develops procedures and specifications, and verifies these. In turn, the construction contractor specifies and installs equipment, and tests and qualifies making systems ready for validation and operation. This process requires that the construction contractor accurately “translate” the operating company’s definitions and expectations into systems, bricks, and mortar. Otherwise, the succeeding steps – development of the validation protocol through change control – will be fraught with problems, delaying time to market.

A Practical Guide to Project Planning

Effective project planning is the key to a successful and cost-effective documentation effort. More importantly, is the integration of construction with C&Q. Operating companies have different preferences: some would award construction and commissioning to the same construction contractor; others would go further and award construction and C&Q to the same construction contractor, ensuring a successful, seamless integration and quality documentation, resulting in the handover of a qualified facility rather than a merely mechanically completed one. (There are additional variations and operating company contracting preferences, which are outside the scope of this article.) The construction contractor’s role in a C&Q project can be broken down into three steps:

- develop and agree upon the scope of work and responsibilities
- agree upon a methodology and develop the project execution plan and quality manual
- develop a project management plan incorporating document management

Each of these steps has components with a significant impact on documentation; therefore, the construction contractor should fully integrate these steps into project planning. The following is a practical guide to each step and its essential components.

Step 1: Develop and Agree Upon the Scope of Work and Responsibilities

At the start of a project, it is essential for the operating company and construction contractor to agree on the scope of work, perform a risk analysis to identify critical and non-critical systems, and identify who is responsible for the various project deliverables, including documentation; the construction contractor also must identify systems and boundaries.

Identify Systems and Boundaries

Working from the operating company’s definitions and engi-

PHASE	DOCUMENT TYPE	ALL SYSTEMS Good Engineering Practice	CRITICAL SYSTEMS Enhance Documentation
Engineering	Design Intent P&IDs Specifications Drawings	B C B C*	V V B V
Construction	Purchasing Vendor Installation	B B C	B C C
Commissioning	Lists Factory Testing Field Testing Start-up Forms	B B B B	B B V V
Operating	Training Maintenance Procedures	B C B	V V V
Regulatory	Applicable Codes Inspection Certificates Permit Documents	B C* B	C C B
Validation	Validation Master Plan Validation Protocols Validation Summary Report	V V V

B: BASELINE DOCUMENT - These documents are created and retained in project records with appropriate project approvals.

C: CONTROLLED DOCUMENT - These documents are created “as built” retained in project files with appropriate project approvals and maintained after commissioning. (Note C* means that only some of the documents in this category require document maintenance)

V: VALIDATION DOCUMENT - These documents are treated as controlled documents, but with the added approvals required for validation programs. Additional approvals usually are limited to Quality Assurance and operations. Document maintenance is a formal change control process.

Table A. Documentation requirements.

neers’ drawings, the construction contractor must graphically delineate each system and its boundaries. This has significance for the organization of the TOP, for example, if it is to be organized by system; it also identifies which subcontractor and/or vendor has responsibility for what element.

Perform Risk Analysis

The risk analysis is an extremely important activity involving the operating company and construction contractor. The result will capture operating company expectations by classifying systems into critical and/or direct impact systems and non-critical and/or indirect impact systems. This is significant because critical systems, such as fermentation, require a higher level of documentation. Thus, the risk analysis culminates in establishing the project documentation requirements - Table A. Documents should be categorized into *baseline* documents, *controlled* documents, and *validation* documents. For non-critical and/or indirect impact systems, Good Engineering Practice (GEP) is considered sufficient while critical/direct impact systems are earmarked for compilation of enhanced documentation packages.

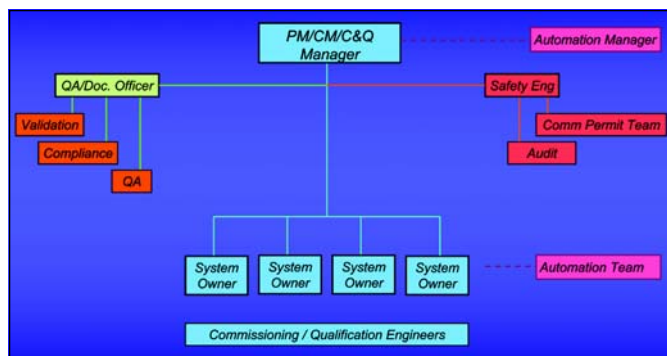


Figure 3. Role of QA/documentation officer.

Name Responsible Parties/Individuals for Specific Activities/Deliverables

With respect to documentation, a hierarchy from “design intent” through to “validation summary reporting” should be established based on the delineation of systems and boundaries - Figure 2. Responsibility for specific documents is assigned to various firms and individuals. Moreover, certain deliverables must be completed before others can start, requiring that these individuals clearly understand their responsibilities, integrate their activities, and effectively communicate with one another. A critical project also benefits from a graphic diagram of the project document hierarchy, which is distributed to each team member. Otherwise, false assumptions might be made and critical documents could “fall through the cracks.” This aspect of Step 1 culminates in two sets of documents: non-FDA regulatory documents (i.e., for reference, archiving, etc.) and regulatory documents.

Identify the Project QA/Documentation Officer

The project QA/documentation officer is a key resource with respect to documentation and must be carefully selected. That is, the project QA/documentation officer’s capabilities must far exceed organizing and distributing documents – he or she must fully understand the regulatory requirements for documentation - Figure 3.

The QA/documentation officer should report to the construction or overall project manager and/or the C&Q manager (either as a member of construction staff or under subcontract if C&Q is performed by a party other than the construction firm) and liaise with the operating company’s validation, regulatory compliance, and QA groups. This individual is charged with ensuring that the operating company’s requirements, policies, and expectations are transferred to all parties involved; confirming that all parties know which documents to produce, and when; and ensuring all the documents are consistent with one another and fulfil the regulatory requirements of compliance, validation, and QA. The QA/documentation officer audits all documentation, including the TOP, ensuring that it can be leveraged to help the operating company streamline qualification.

In essence, the QA/documentation officer must effectively align the contractual expectations of the operating company and construction contractor. While some operating compa-

nies prefer to hire a third party, the advantages of hiring a construction contractor with this in-house capability are greater consistency, compliance, and speed.

Step 2: Agree Upon a Methodology, and Develop the Project Execution Plan and Quality Manual

Well before design is completed, the construction contractor and operating company should agree upon a qualification methodology. Based on this, the construction contractor will identify standard operating procedures; develop a schedule, commissioning plan and validation master plan; and also agree on the level of leverage from commissioning into qualification. These, among other strategies, will be used to determine the organization of the TOP. Leveraging can be defined as the utilization of properly documented activities carried out during construction and commissioning which can be used in support of qualification (IQ and OQ) resulting in the avoidance of unnecessary repetitions hence reducing qualification time.

Identify Standard Operating Procedures (SOPs)

The construction contractor must identify and define all SOPs, including protocol formats, numbering systems, and the review and approval process. This ensures that proper procedures are in place to document all systems and components for the TOP. The construction contractor must maintain consistency among numbering systems used by the various suppliers and align these with the operating company’s requirements for the project. Ultimately this important component of the methodology and project execution plan ensures a smooth compilation of the documentation and TOP.

Develop a Project Schedule Capturing Commissioning, Qualification, and Validation

Development of a project timeline by the construction contractor identifies the required resources and critical timings for data or documentation that are required for subsequent activities to proceed. This is critical to streamlining the process.

Develop Commissioning Plan

An important component of the project methodology is the commissioning plan, which identifies the level of documentation appropriate for commissioning, level of quality, and required signatories based on the operating company’s qualification strategy. For example, some operating companies use an Integrated Commissioning Qualification (ICQ) strategy, in which much of the commissioning documents will be leveraged into the qualification effort, thereby reducing time to market - Figure 4.

Develop Validation Master Plan

The validation master plan, including computer systems validation, must be aligned with the commissioning plan and operating company’s qualification strategy.

Determine Organization of TOP

Based on the strategies of C&Q, the construction contractor must determine the proper organization of the TOP and what level of documentation is required from the various parties. The organization of the TOP is critical to the success of the qualification process – that is, it must be organized in such a way that the operating company is able to leverage the documentation and data into qualification. In effect, the TOP aligns the contractual responsibilities of the operating company and construction contractor. The TOP signifies the end of an important phase and a handover to the operating company. In some cases, the TOP could signify the end of mechanical completion, where design and construction data is turned over to the operating company; in others, it signifies the completion of commissioning and qualification - Figure 5.

The TOP consists of specifications, manuals, drawings, and other documentation that fully characterizes each system or piece of equipment installed in the facility. The construction contractor should prepare a TOP matrix for each system, which defines the documentation required for all its components. Compiled in a formal and organized package, the TOP serves as part of the basis for Installation Qualification (IQ), which verifies that the physical components of the system have been installed according to design specifications. As the final major component and system quality audit prior to Operation Qualification (OQ), the IQ is a critical step that lays the foundation for compliance and testing of the facility.

In fact, the TOP is critical throughout all phases of the project – from design and procurement to handover at mechanical completion, commissioning, or qualification. Thus, each of the following activities must be carried out to ensure documentation of compliance:

- **Design and Procurement Phase:** the construction contractor’s team must review the design of the project for system boundary demarcation, regulatory requirements, commissionability, Good Automated Manufacturing Practice (GAMP), and Code of Federal Regulations (CFR) 21 Part 11 compliance, and to develop the templates for commissioning, Factory Acceptance Testing (FAT), Site Acceptance Testing (SAT), and qualification documents. The commissioning plan and validation master plan are developed and delivered in this phase. Members of the team responsible for commissioning must review Piping and Instrumentation Diagrams (P&IDs) and 3D design models for safety and the inclusion of commissioning requirements. They also will attend Hazard and Operability (HAZOP) and constructability reviews, as well as design specifications and procurement documentation to assure that the requirements of the operating company are included and delivered.
- **FAT:** during the procurement phase, the construction contractor should ensure that a determination is made as to which equipment will undergo formal FAT. Items which

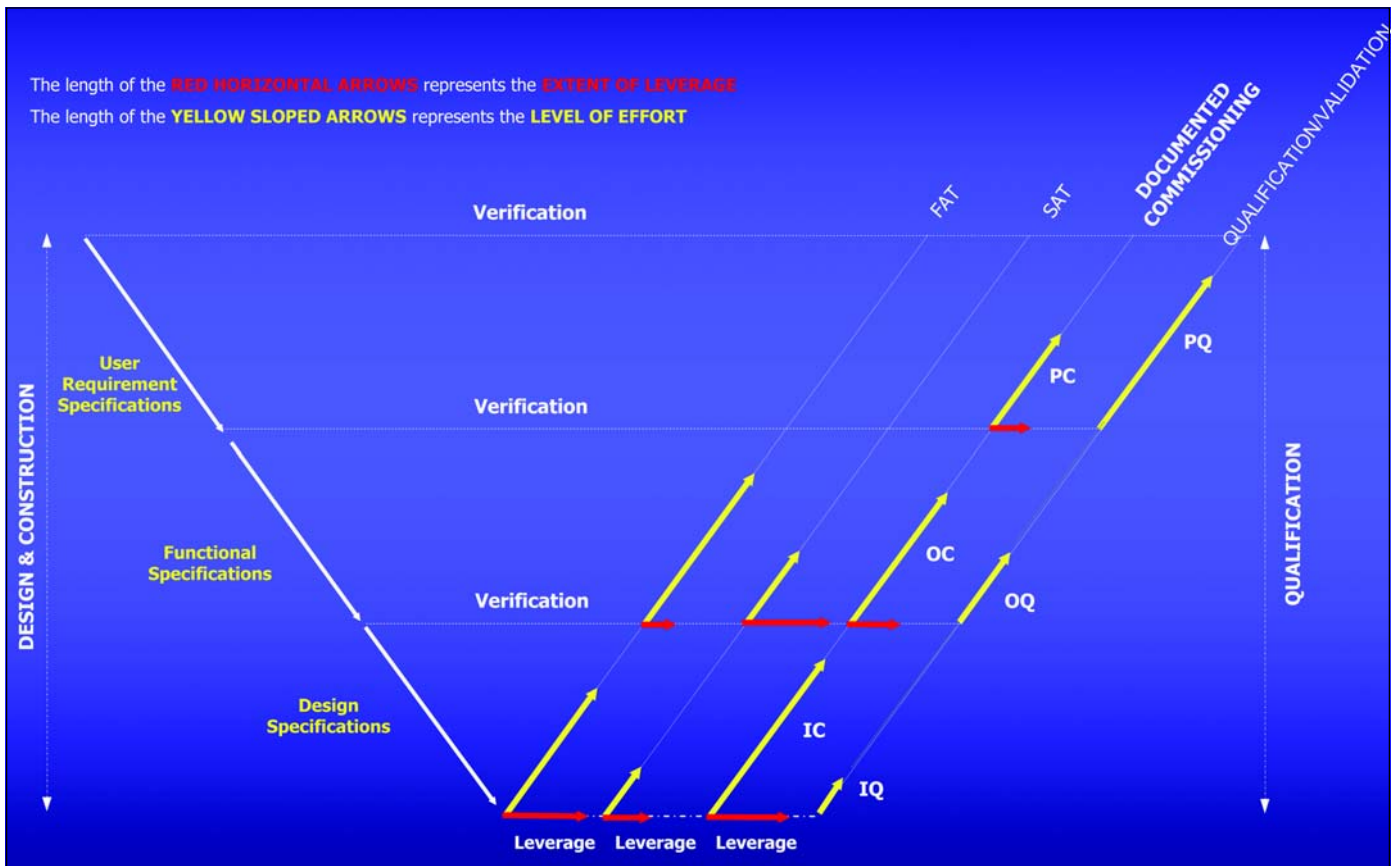


Figure 4. Leveraging commissioning into qualification.

Commissioning and Qualification

cannot undergo “FAT” should be subjected to a “document and component verification.” For the selected items, the construction contractor must develop and issue FAT test protocols. The construction contractor’s FAT team, led by the individual who is responsible for commissioning, will execute the FAT in the vendor’s facility. The commissioning head must verify that the equipment complies with the User Requirement Specifications (URS) and design specification, and that all documentation for operation, maintenance, and qualification are complete and available. Functional testing is generally undertaken for information and engineering verification purposes only. Programmable Logic Controller (PLC) functionality must be verified, as well as the data communications to the plant supervisory systems to ensure their compatibility and transmission. Finally, documentation, controls hardware, and the component schedule must be formally verified because these will be subsequently used to leverage the IQ.

- **Construction:** during construction, the project team will audit construction of each system and witness primary construction activities, such as loop testing, pressure testing, and flushing. The team also coordinates vendor installation checks and verification of SAT readiness. In addition,

the bulk of the commission and qualification documents are generated and issued for approval during the construction phase. A number of construction activities must be documented, as well as witnessed, to meet Good Manufacturing Practice (GMP) requirements (e.g., welding of sterile piping and verification of slopes) and will be used to leverage the IQ. By working closely together, the QA/documentation officer, supporting staff, and construction team can expedite the handover from construction to commissioning – speeding time to market.

- **SAT:** the construction contractor typically splits the SAT into two phases – an installation and documentation verification phase and a functional testing phase. An audit of the FAT documentation and schedule checks is performed to verify that no changes have occurred since the FAT (i.e., the FAT data is still valid for the IQ). During functional testing, the system is tested, coupled with the actual site utilities, and linked to the site supervisory system for full data transmission functionality.
- **Commissioning:** in the pre-commissioning phase, the construction contractor performs final hot-loop checks and instrument calibrations, as well as motor and device run-in tests. The construction contractor is responsible for the

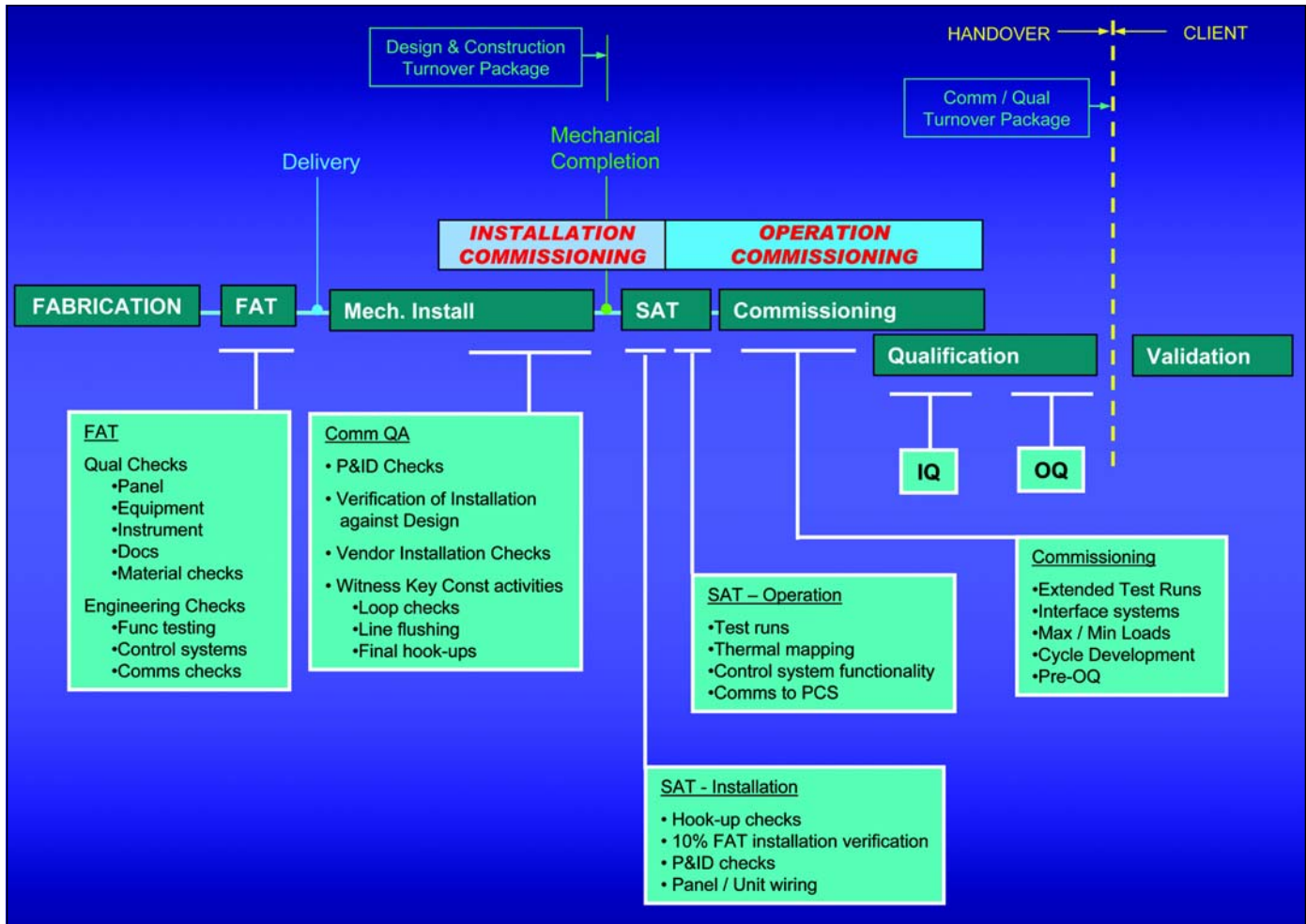


Figure 5. TOP’s critical role in all project phases.

execution of the commissioning procedure and IQ protocol. During commissioning, each system is tested in conjunction with other interface systems for the functionality as required by the URS and specifications. Toward the end of the commissioning phase, the construction contractor performs a pre-run of the OQ testing to “de-bug” and provide assurance of a successful OQ execution. During commissioning, the construction contractor may perform an expanded level of testing of system functionality (i.e., in excess of the OQ requirements) to test the limits of system capabilities. It is important to note that not all of these tests will necessarily need to be documented – the construction contractor and operating company should discuss and agree upon the extent of documentation required as part of the commissioning plan and its documentation requirements.

- **IQ:** following the SAT and pre-commissioning, the construction contractor performs system IQ. Much of the verification data from FAT, construction, SAT, and pre-commissioning can be leveraged into the IQ if it has been effectively documented, which saves the operating company valuable time - *Figure 6*. The QA/documentation officer is responsible for the verification of the IQ support documentation files from the various project phases.

- **OQ:** a separate standalone OQ should be performed to enable the commissioning procedure to be segregated from the formal qualification files. A pre-run of OQ testing in the commissioning phase ensures a successful OQ, which will reduce deviations and streamline the OQ process and its documentation.

Plan for Integration of Construction, Commissioning, Qualification and Validation

The construction contractor normally is focused on getting the facility built and started up. However, the construction contractor’s overriding goal must be the integration of *all* field activities with respect to documentation – the success of the qualification and validation process ultimately depends on the quality of documentation at each step. Typically, documentation is divided into two categories — project files and qualification files - *Figure 6*.

The project files are handed over to the operating company for reference and archiving; they will not compose part of the qualification package. The qualification files are controlled documents, which fall under the change control procedure; therefore, these must reflect greater attention to the URS, specs, vendor audit, validation master plan, and project plan. From a regulatory perspective, if the engineer, construction contractor, or operating company makes any changes to the

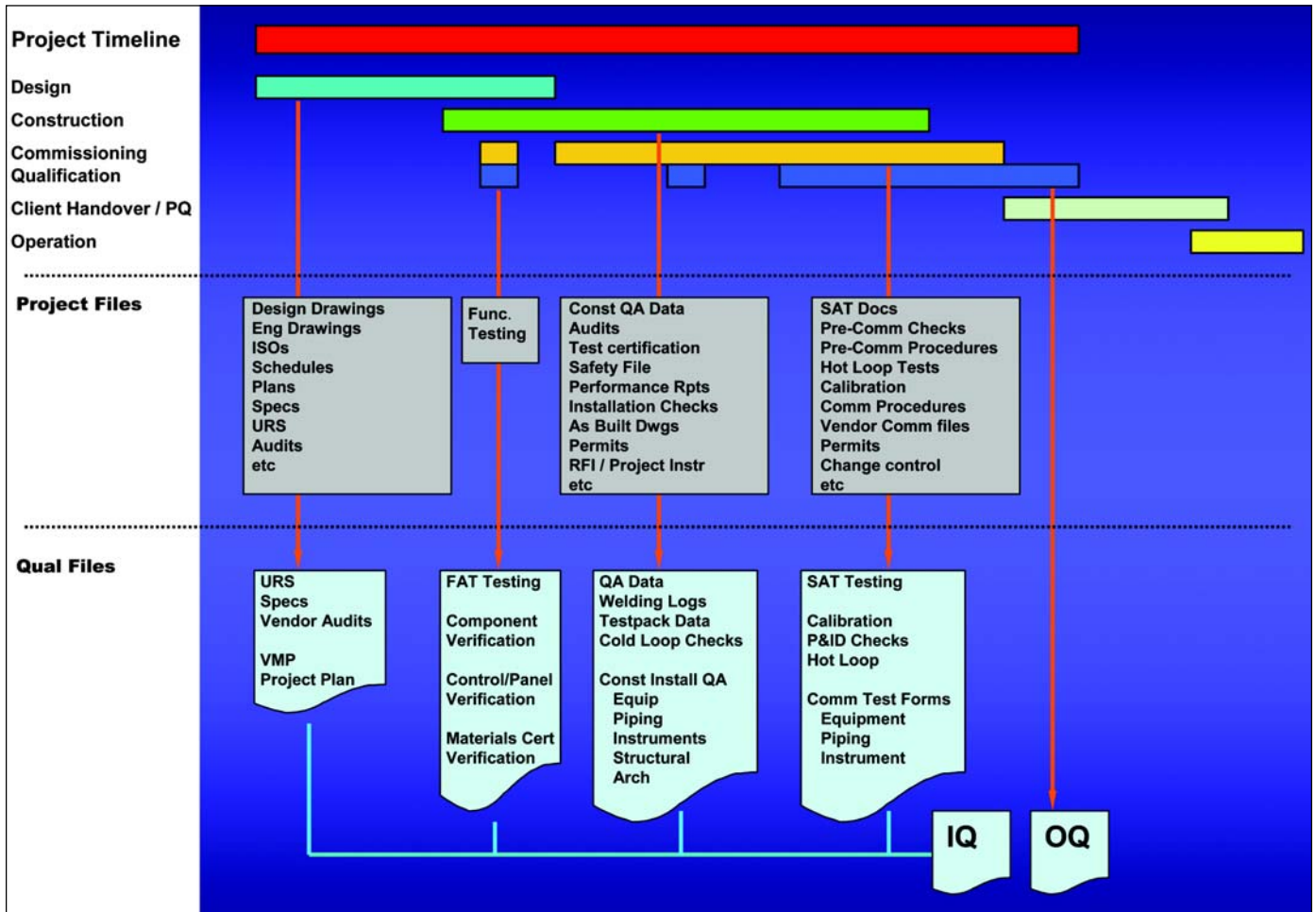


Figure 6. Integrated documentation (project and qualification files).

systems, the qualification files must be updated so that they reflect the validated standards of the operating company's facility. Associated with the handover of documents to the operating company, the construction contractor should set up operations and maintenance training for the operating company's key personnel, as well as document training for the entire project team. The construction contractor also should be involved in change control and deviation management.

Step 3: Develop a Project Management Plan Incorporating Document Management

Considering the voluminous documentation gathered and developed during the course of constructing, commissioning, qualifying and validating a modern pharmaceutical or biotech manufacturing facility, the control, tracking, and data storage mechanisms employed to amass these materials have become indispensable tools for efficient and successful project management.

Document Control, Review Cycles, and Approvals

In a successful project, document control is not the sole responsibility of a single individual. Instead, it is a team effort that requires early involvement of all the participants – engineers, project managers, vendors and sub-construction contractors, commissioning, qualification and validation groups, including their technology leads. Policies, practices, and procedures developed by this team must be rigorously adhered to by all parties throughout the project. The construction contractor's role cannot be understated — even procurement documents gathered in the early stages of the effort will become an important part of the TOP that will support the licensure and regulatory approval process.

If the operating company already has established document practices, procedures, and change control policies in place, the construction contractor should establish document methods for distribution, review cycles, version control, numbering, and approvals that mesh with these practices. The construction contractor may use an electronic document control platform to create distribution groups for recipients of various types of documents and control different versions of documents as they are developed, recording all relevant comments and the names of their originators.

Data Security

The operating company should ensure that the construction contractor is prepared to physically secure and store critical original hard-copy documents in fireproof cabinets, and ensure that electronic versions of these documents are backed up regularly on two systems in two separate locations. Often, the construction contractor's project managers will ensure that copies of critical project documents are maintained at three locations.

Reducing Time to Market

High-quality documentation is essential to achieve regula-

tory compliance. The construction contractor must appreciate the significance of documentation, and make it an integral part of the construction planning, implementation, and commissioning process from the inception of the project. The construction contractor's goal is not only to build a facility on time and within budget with systems that perform to specifications – it is also to develop a TOP that is well organized, meets the operating company's unique needs and expectations, and provides the proper level of documentation quality. When the construction contractor effectively manages the construction and commissioning documentation process, the operating company can leverage the resulting documentation for the qualification process, reducing time to market.

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