

Effective Computerized System Compliance through Leveraging Supplier Effort

by Members of the ISPE GAMP® Leveraging Supplier Effort Special Interest Group

This article describes a controls framework that can be used to assess risks and determine a validation strategy that leverages supplier effort appropriately.

Introduction

Regulated customers face increasing pressure to utilize resources efficiently while ensuring effective compliance with global regulatory requirements in order to ensure patient safety, product quality, and data integrity. Effective and efficient compliance is established through process understanding, understanding of patient/product risk, adopting a scalable lifecycle approach, maximizing subject matter expertise, and avoiding duplication of effort. ISPE GAMP® 5 recognizes the key role of product and service providers in meeting these criteria.

Recognizing the capabilities, experience, and willingness of suppliers and integrating regulated customer and supplier resources provides an opportunity to utilize their combined knowledge, effort, and documentation to effectively achieve regulatory requirements. Leveraging supplier effort enables:

1. Targeting of internal resources on areas of greatest risk to patient safety, product quality, and data integrity
2. Minimizing duplication of effort between suppliers and regulated customers
3. Accessing subject matter expertise to ensure that solutions are fit for purpose and decisions are based on knowledge and quantifiable risk

All of these objectives are in line with the GAMP® 5 principles to leverage supplier effort and to focus patient safety and product quality risks. Further, GAMP® 5 promotes the role of the subject matter expert in order to ensure that solutions are appropriately specified, implemented, and verified. Suppliers to the industry are a valuable source of such subject matter expertise.

Supplier assessment is a means by which regulated customers evaluate the effectiveness of product development and support systems to assist in planning system implementation, validation, and operational compliance requirements. Where the supplier's quality management system reflects pharmaceutical industry guidance, such as ISPE GAMP 5 or other cross industry standards/guidelines, such as ITIL®, COBIT®, TickIT®, etc., there is greater opportunity to leverage supplier effort. The extent of management and verification control applied by the regulated customer will be influenced by the outcome of the supplier assessment, the criticality of the business process, and the potential impact the supplier product or service has on patient safety, product quality, and data integrity.

This article does not set new expectations with respect to supplier quality practices; rather it presents an opportunity for regulated customers to establish risk-based controls that ensure mutual understanding of objectives and effective planning, management, and verification of supplier input to validation and operational compliance processes.

This article describes a controls framework that can be

used to assess risks and determine a validation strategy that leverages supplier effort appropriately. In designing the controls framework, it is recognized that there is no “one size fits all” solution to leveraging supplier effort. Suppliers, and indeed regulated customers, operate to different business drivers, standards, and tolerance of risk; the controls framework simply identifies potential controls that should be selected and adapted accordingly.

What is Leveraging?

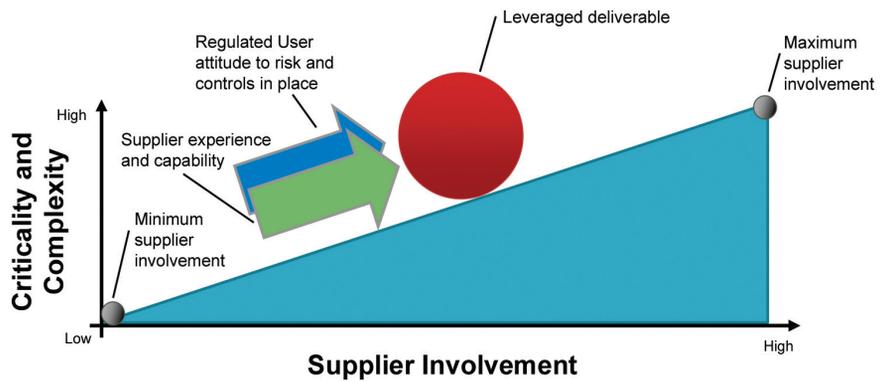
In the context of this article, supplier means product suppliers, support organizations, service providers, and internal supply organizations, such as IT/engineering and similar organizations at any phase in the system lifecycle.

In the context of this article, leveraging is the utilization of supplier “artefacts” (supplier skills, knowledge, and documentation) in support of the regulated customer’s compliance activities throughout the life of the computerized system (implementation and operation). Looking at the activities, knowledge, and responsibilities for both supplier and regulated customers, it becomes clear that there are two significant opportunities to leverage supplier effort.

First, duplication; there is overlap between the project activities of the supplier and regulated customers, in particular in the areas of planning, specification, testing, and support. An opportunity exists to remove duplication of effort and find more beneficial ways of verifying what has been done by others.

Second, skills and knowledge; with the experience of suppliers implementing similar solutions across a broad range of organizations, there is an opportunity to leverage such knowledge in support of effective decision making, solution development, project activities (e.g., requirements definition, risk assessment) and documentation creation.

It should be recognized that leveraging supplier effort does not, of course, affect the accountability for compliance. This always resides with the regulated customers. Leveraging cannot be undertaken blindly. It requires focused planning to assure the capability of the supplier and verification of any artefacts that may be leveraged. Supplier assessment for critical applications may become more intensive, in terms of verifying



The slope increases with increasing criticality and complexity of the solution, implying that the capability of the supplier and the regulated customer’s controls must increase.

Figures 1. Determining the leverage position for a deliverable.

specific outputs of supplier quality management systems, rather than being a general appraisal. For example, where supplier testing is to be leveraged, the supplier assessment process may include a more comprehensive assessment of the effectiveness of critical function testing processes and documentation.

The Keys to Effective Leveraging

In order to leverage supplier effort, there needs to be a consistent understanding of expectation, capability, and risk between the regulated customers and supplier. Effort expended in the planning, evaluation, and specification phase will ensure that the benefits of consistent understanding are felt throughout project execution and operation.

The supplier influences the extent of leveraging through

Control Type	Objective of Control	Examples
Planning	Ensures the right activities are being undertaken and decisions being made at the right time by the right people	Ensure deliverables of different suppliers are synchronized Ensuring supplier and regulated customer’s validation activities are integrated Addressing outcome of supplier assessment
Evaluation	Ensures that supplier knowledge, effort, and artefacts are only leveraged based on understanding of supplier capability and quality	Supplier Assessment Establishing mutual understanding of system requirements
Subject Matter Expertise Input	Ensures that people with appropriate expertise provide input into activities, deliverables, and decisions. Such people should have required experience, the authority to make decisions, and should be available to provide input and make decisions in a timely manner.	Ensure technical experts are engaged in design and design review Ensuring system requirements reflect current and/or planned business processes, are complete and accurate, and reflect experience of previous implementations Ensuring test teams understand business processes and good testing practice
Verification	Ensures activities and deliverables are confirmed as being fit for purpose	Review of design Ensures appropriate Testing of implemented solution Review of supplier test records

Table A. The controls framework recognizes that there are different types of control.

the effectiveness of their quality systems, experience, and capability. The regulated customer's attitude toward and ability to leverage is influenced by the criticality of their business processes, their attitude to risk, effectiveness of project management, and quality processes and internal skills and capability - *Figure 1*.

Controls Framework

Armed with a clear appreciation of the capability of both supplier and regulated customers, the project team will be ready to utilize a controls framework. The controls framework identifies typical controls that may be applied to ensure supplier activities, knowledge, and artefacts are appropriately leveraged. The identified controls ensure that supplier activities are appropriately planned, managed, and verified according to business process criticality, project/system complexity, and supplier capability - *Table A*.

The controls framework is intended as a guide only. An alternative set of controls may be appropriate, based on the characteristics of the supplier services being provided and regulated business operations being supported; however, the criticality of a system should not preclude leveraging; rather the controls applied need to be commensurate with risk. The controls framework encompasses three stages in the life of a computerized system, including planning, implementation, and operation.

Stage 1 – Planning

Development of the controls framework reinforced the fundamental importance of understanding project enablers and setting expectations, both within the regulated customers

and with potential suppliers. Early planning and evaluation will determine the extent to which supplier knowledge, activity, and/or documentation can be leveraged. Activities such as supplier assessment, due diligence, project tendering, project/validation planning, contractual agreement, and previous experience shall determine:

- Willingness to cooperate and level of trust between parties
- Supplier capability, knowledge, and experience in the context of proposed project/service
- Mutual understanding of business processes/operations and risk
- Technical competency
- Effectiveness of quality systems
- Flexibility of supplier and regulated customer's quality systems in enabling (even encouraging) leveraging
- Quality of supplier deliverables
- Supplier longevity and client relationship
- Experience of previous projects/operations of similar characteristics
- Intellectual property considerations
- Degree of deviation from normal supplier practice

At the outset of any cooperative relationship, it is important to gain mutual understanding of:

- Project certainties and unknowns
- Supplier and regulated customer's roles and responsibilities
- Business process and user requirements, including deficiencies

Activity	Accountable Organization (Typical)	Opportunity for Supplier Input	Potential Regulated Company Controls (in addition to general controls)				Potential Risks and Considerations
			Planning	Evaluation	Subject Matter Expertise	Verification	
IMPLEMENTATION							
Validation Planning	Regulated Company	Input to Validation Plan, integrates Supplier and Regulated activities Integrate Supplier Quality Plan and Regulated Company Validation Plan	Reference in contract documents Integrate quality/validation activities into project plans Where supplier records are to be verified but not owned by the Regulated Company, controls need to be established to ensure integrity, access to and retention of such records for the required retention period	Evaluate previous examples Evaluate Supplier Quality Plans	Regulatory and Industry Knowledge	Review and approval (and ownership) of Validation Plan Review and Approve Supplier Quality Plan Define Verification Activities	Loss of knowledge within Regulated Company Regulated Company maintains overall Quality Assurance and Verification Accountability May necessitate increased number of supplier meetings/verifications

Table B. Detail of the controls framework for validation planning.

- Quality systems and regulatory standards that will apply
- Controls that will be applied by both parties to manage the project/service, including verification controls
- Expectation of deliverables and ownership of deliverables
- Knowledge transfer requirements
- Ongoing support (including regulatory inspection)

Stage 2 – Implementation

The second stage of the controls framework examines controls from validation planning, through to completion of validation reporting. It is clear that some deliverables fall into natural groupings with a single set of requirements and controls; for example, the controls for each of the testing phases are likely to be similar. The supplier may be engaged to plan, specify, and execute tests with the regulated customers providing input, review, and oversight of testing.

Stage 3 – Operation

Activities during operation of the computerized system may provide opportunities for further leveraging of supplier knowledge and effort in areas such as change management, configuration management, repair, back up, and restoration and disaster recovery. Leveraging during the operational phase is likely to require greater integration between supplier and regulated customer's support organizations and

quality systems. Establishment of service level agreements defining roles of supplier and regulated company organizations, service management controls, service performance expectations, and quality systems requirements are fundamental to service management.

In Table B, the traditional approach to validation planning is for the regulated customers to create, review, and approve the validation plan with the supplier, perhaps reviewing the validation plan initially during the tender process. In a leveraging model, the supplier may provide significant input into the validation plan, addressing system validation aspects; however, accountability for validation of the overall business process must remain with the regulated customer. Such an approach may ensure greater or clearer integration between the supplier and regulated customer's activities.

Secondly, the case of specification is described in Table C. Traditionally, the regulated customer develops the user requirements specification and issues this to the supplier for review and response during project tender processes and design processes. However, a supplier organization may have experience of previous implementations, skills in capturing and analyzing requirements from other customers, or tools for articulating and demonstrating requirements accurately and without ambiguity. Recognizing that a regulated company will require at least an initial understanding of

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			Planning	Evaluation	Subject Matter Expertise	Verification	
IMPLEMENTATION							
Business Process Definition and Requirements	Regulated Company	Experience of previous implementations Skills in defining clear, complete, accurate requirements Technology experience	Reference in contract documents	Evaluate previous examples	Provide knowledge of "AS IS" processes Provide initial "TO BE" processes and requirements	Review and approval (and ownership) of Business Processes and Requirements	Loss of knowledge within Regulated Company Regulated Companies must own business processes and requirements and understand business/regulatory risks
Functional Specification	Supplier	Expertise in system implementation Create Functional Specification Provide Traceability to Business Processes and Requirements	Input Business Processes and Requirements		Input to Functional Specification	Review and approval of Functional Specification Review Traceability to Requirements	Typically a supplier led activity, limited opportunity for further leveraging
Detailed/System Design	Supplier	Expertise in system implementation Create Design Provide Traceability to Product or User Requirements	Input Business Processes and Requirements (if customizations required)		Provide business and IT input (if customizations required)	Testing based on Business Process and Functional Risk Assessment	Activity that is evaluated during supplier assessment, limited opportunity for further leveraging

Table C. Detail of the controls framework for specification.

their business processes and user requirements in order to effectively select a solution, leveraging supplier experience and expertise earlier in the ongoing development of user requirements could lead to a more effective solution with reduced risk for misunderstanding.

Other considerations are identified within the controls framework, providing additional experiences that should aid the reader in considering appropriate controls. For example, during the testing phase, “other considerations” for leveraging supplier test documentation would include the degree of customization required to implement business processes. An “out of the box” supplier test package would be less useful to the regulated customers when there is a high degree of system configuration and/or customization.

Practical Considerations

When using the controls framework:

- Greatest benefit may be achieved if both parties work to their own established QMS with no additional controls other than interfaces between supplier and regulated customer’s QMSs.
- Suppliers will have certain strengths and weaknesses; therefore, it should not be assumed that all supplier knowl-

edge, activities, and documentation can be leveraged.

- The extent of leveraging may change as more knowledge is developed during the delivery of the project or service.
- Where several suppliers are involved in a project, there will be a unique controls framework for each of them, given the nature of the relationship, experience, expertise, etc., between the regulated customers and each supplier.
- The ability to leverage from one supplier does not imply that knowledge, activity, or documentation can be leveraged from all suppliers.

ISPE Members can download the controls framework from the ISPE GAMP® COP website (www.ispe.org/gampcop).

During the creation of this article, a revised EU GMP Annex 11 was published. ISPE GAMP has published an interpretation of Annex 11, mapping requirements to GAMP 5. Annex 11 highlights key considerations for external and internal suppliers that are discussed in the interpretation article. Key highlights are found in Table D.

Regulations in the US, such as 21 CFR 211.34, recognize where consultants advising on manufacture, processing, packing, or holding of drug products are required to be sufficiently trained, experienced, and educated with records kept. FDA’s General Principles of Software Validation (11 January 2002)

make reference to regulated customers “assess[ing] the adequacy of the software developer’s activities and determine[ing] what additional efforts are needed to establish that the software is validated for the device manufacturer’s intended use.” The manufacturer has latitude and flexibility in defining how validation will be accomplished. Supplier provision of information about their system’s requirements, testing process, and results of their testing can be used by the regulated customers as the basis for their validation activities.

Knowledge Transfer and Accountability

Leveraging supplier knowledge, effort, and documentation infers greater dependence upon suppliers. It is essential that regulated customers recognize and address key issues:

- Regulatory compliance is a sole accountability of the regulated customers
- Regulated customers must understand their business processes and business/compliance risks
- Regulated customers must be able to defend their compliance position

Topic	Key Considerations
Documentation	Agree with provision of documentation, this includes supplier and regulated customer’s documentation, which should be highlighted in the validation plan or similar document (e.g., document management plan).
Risk Management	Where there is a large third party involvement, opportunities for sharing data, control information, quality standards and records, based on a justified and documented risk assessment, should be taken. Trust and confidence in suppliers will enable the leveraging of material and the avoidance of duplication of effort.
Compliance	Requirements for third party suppliers and service providers are extended to internal IT departments (as they are regarded as “analogous” to third party suppliers in this context).
Validation	Annex 11 requires “manufacturers,” i.e., suppliers, to be able to justify their standards, protocols, acceptance criteria, procedures, and records based on their risk assessment. It would be sensible for each party to list and index such documents linked in the formal agreement or validation plan
Change Control and Deviations	Record keeping requirements during the project validation phase may (for complex projects) result in a high level of cooperation to enable review and transparency. The level of cooperation should be spelled out in the formal agreement between parties to the project. Section 4.2 concerns evidence, in support of fitness for purpose, that suppliers are required to provide.
Supplier Assessment	Section 4.5 specifically refers to the need for a formal assessment of the supplier, as a means of demonstrating that all reasonable steps have been taken by the regulated customers to ensure that the system has been developed in accordance with an appropriate QMS. It is likely to be to suppliers’ advantage to demonstrate fitness for purpose in this regard.
Custom/ bespoke computerized systems	Section 4.6 requires the formal assessment and reporting of quality and performance measures for all the lifecycle stages of these systems. Where integrators and other contract staff are involved, then control, coordination, and cooperation are essential. The validation plan should make clear just how these aspects of the project will be covered. The formal agreement should cover data and knowledge sharing.
Testing	Section 4.7 provides an opportunity for the sharing and leveraging of supplier and customer knowledge and methodologies on evidence of appropriate test methods and scenarios. Automated testing tools and test environments are expected to have documented assessments for their adequacy. While these aspects would normally be covered by the validation document set, where such records reside primarily at the supplier, then original relevant information may need to be made accessible to the regulated customers as evidence in support of the specific compliance requirement.

Table D. Annex 11 highlights key considerations for external and internal suppliers.

- Business agility should not be constrained by supplier relationships

Conclusion

For both regulated customers and suppliers, adopting this approach to leveraging will enable:

- Understanding of project/service objectives
- Mutually agreed specification
- Understanding of roles and responsibilities
- Earlier realization of business benefits of the solution

Suppliers will further benefit from working to their own internal standards and tools. For the regulated customers, additional benefits of adopting this approach are:

- Access to expertise and experience
- Avoidance of duplication
- Focused use of internal resources in critical areas
- Managing the effect of losing internal knowledge through effective supplier relationship
- More effective solutions

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