Identifying Benefits for S-88 and S-95 Based Systems

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ABSTRACT
System Architectures using S-88 and S-95 standards are being used in system implementations across the plant floor. These systems include batch management, MES, process control and ERP integration. For regulated industries, electronic record keeping and system validation must be addressed in these new initiatives.

When implemented as applications, these architectural components are designed to provide benefits that support the company’s business drivers. These benefits often overlap as the interfaces between applications become blurred as application vendors are changing functionality.

Using S-88 and S-95 standards and an architectural approach, system requirements can be related directly to benefits. This paper presents system life cycle architecture for implementing pharmaceutical automation projects. Primary, secondary and strategic benefit sources for measurable economic benefits in each functional area of regulated and non-regulated operations. Realized benefits are presented for actual implementations across the plant floor.

Identifying and Quantifying Benefits?
Measurable economic benefits for pharmaceutical projects can be classified as primary, secondary or strategic. Primary benefits are realized when the project is executed and put into use. Not doing the project means that the benefits will not be realized. Secondary benefits occur in other organizations as a result of the project’s activities. These benefits should not be ignored in determining the merits of the project, as they can be
substantial. An example is the savings in people and efficiency in the Documentation Department that results from implementing an electronic batch record system for a new plant. Strategic benefits should also be factored into the cost/benefit analysis. Enhanced compliance, maintaining a market share in a specific therapeutic area or opening a plant in a new geography may be necessary while the value may be intangible. Often secondary and strategic benefits are ignored, as they do not have an exact value. Accountants sometimes would rather be exactly wrong than be vaguely correct.

As projects involving mission critical applications will define a competitive edge for a company, specific results become company confidential and are difficult to obtain as they indicate internal financial structures, overhead rates and product costing. Available benefits from actual projects presented as percentages are available and can be applied to your own business model as they can be used to develop quantitative values once you have identified similar business issues.

Project planning for pharmaceutical systems must include support for computer system validation. System Development Life Cycle (SDLC) methodologies provide an excellent framework for these computer-based projects. An SDLC is identified as a life cycle for the development of the integrated systems and includes the physical components and collection of principles, models, standards and guidelines that are the core building blocks for the system infrastructure. A SDLC methodology is a mechanism to identify, qualify, and quantify benefits with respect to reducing project design and implementation schedules as being the Master Validation Plan for the project implementation. Incorporating standards, architectural analyses and integrating the organizational and documentation requirements, project management can create a project plan to achieve the identified benefits while controlling resources, the budget and schedule. The focus of the paper is where benefits can be identified and quantified to support the project justification, which occurs during the initial phases of the SDLC. The investigation of benefits should be based upon a system implementation framework for the project through out its development life cycle (Ref. 1-4).

**Computer System Validation**

The FDA definition of process validation is contained in the “General Principles of Validation guideline (Ref. 5) as,

> “Establishing documented evidence which provides a high degree of assurance that a specific process will consistently produce a product meeting its predetermined specifications and quality attributes.”

The FDA has no formal definition of computer system validation and expects the definition of validation to apply equally to manufacturing control processes involving computers and other types of automation equipment. The Pharmaceutical Research and Manufacturers Association (PhARMA; formerly the PMA) developed a life cycle approach to computer-related system validation (Ref 6). This effort defined a process for defining, developing and quality testing of new and existing computer systems. The Parenteral Drug Association’s (PDA) Validation of Computer-Related Systems Report (Ref. 7) defined a method emphasizing comprehensive functional and design documentation. Like the PhARMA and PDA methodologies, an SDLC can cover all phases of system operation as it integrates the information, human and organizational and manufacturing equipment architectural components into a unified validation master plan. Performing analyses to derive business benefits are an integral part of the plan. These activities are established early in the project and supported throughout the development and implementation phases.
Required validation documentation is identified or developed at each phase. During the Concept phase, QA validation policies and SOPs are reviewed for applicability and the validation program plan and guidelines developed.

The PDA validation master plan fit very well within an SDLC architecture. The manufacturing component contains the physical process equipment lines, computer systems, networks, hardware controllers, operator work stations, control room functions, operator control panels and software applications. Any infrastructure or design standards like S88.01 and S95.01 are integrated into the development process.

The human and organizational component defines the involvement of people in the new system. The boundaries of how much automation will be implemented on both the physical and information sides of the system are fully defined and documented. Often, the changes in people skill sets needed to support the new systems are not addressed during the early life cycle phases.

The information architecture catalogues the validation documentation needed to describe each phase of the project; the information systems needed to support the process (e.g., batch record recording, SOPs, QC test results, etc.) and the system performance parameters, production batch record information and operator instructions. Training plan, certifications and educational development are planned, designed and refined as the phases progress. We have all of the information for a successful and complete validation of the completed system. Nothing has been missed.

**Concept and Definition Phases: Business Processes**

The business process planning starts with the company’s business plan. The vision for the proposed CIM project is considered in context to the corporate mission and vision objectives. The concept and definition phases define and clarify the organization’s business objectives and the related elements that are critical to achieving these objectives. Taken together, these constitute the “as is” of the business or where we are today and the “to-be” environment, which represents the enhanced business state. The analyses and documents collected, catalogued or developed during this phase are given in Figure 1.

The phases define how the company’s business mission, measurable business objectives, critical success factors, and strategies impact the project and how the project will support the business goals and achieve measurable economic benefits. By answering questions like in the following list, the project team will be able to determine quantitative benefits like increase in yield, cycle time reduction, enhanced quality assurance and reduced validation resources,

- What and how are we doing today?
- What is our business mission?
- What business objectives will achieve this mission?
- What are the critical successes factors that do we have to do right in order for these objectives to be achieved?
- What business strategies will need to be deployed to ensure that we achieve these critical success factors?
- How can we measure success and when can we stop?
Identifying Benefits

Key sources of potential benefits can be achieved from a number of sources like,

- Using the SDLC as the tool for implementation
- Using infrastructure and design standards
- Integrating the organization into the project plan
- Installing applications provide specific economic benefits in functional areas and
- Integrating cross-functional operations between the enterprise’s business processes and manufacturing’s operations

SDLC Benefits

Adler, (Ref 8, pp. 62-64), and Williams and Adler, (Ref 9, pp77-78), present some interesting multi-year cost/benefit results. They describe an automation life cycle model used at Eli Lilly to meet bulk manufacturing costs while being cost competitive. “The model forces those in charge of automation to look at both the front half of the life cycle—justify, apply and install—as well as the back half—operate, maintain, and improve” … “Here is why! Data from ten major facilities at Eli Lilly indicate that less than 50 percent of the life cycle dollars deliver a project. That’s where 25 % of the benefits of automation come from. An important aspect of automation is that one needs to make another 50 or 60 percent investment over the life cycle to get 75 percent of the benefits of automation.”

Use of Standards

Infrastructure standards are being used in pharmaceutical strategies because timely, accurate and auditable information is essential in this highly regulated industry. An I/T framework has to support business objectives by being flexible, capable of growing to meet increasing demands for information and reporting and permit the sensible inclusion of new information technology that may be required by manufacturing. As an example, using PROFITBUS as the project infrastructure technology, process automation installation costs were reduced approximately 40% with projected reduced maintenance costs over the life cycle of the installation (Ref 10).

ANSI/ISA S95.01 standard (Ref. 11) defines the interface content between manufacturing control functions and other enterprise functions. The standard has been approved and is available on the ISA’s web site. S95 Part 1 contains a collection of business drivers that are critical to the success of manufacturing operations across a variety of industries, see Figure 2. They include customer-driven quality requirements and
operational requirements such as productivity, cycle time, deployment of new technology, strategic alliances, supplier development, and research and development.

![S-95 Business Drivers](image)

Figure 2 ISA S-95 Business Drivers

If any of these business drivers is applicable within the manufacturing organization, it becomes the focus for determining project-related benefits that justify the automation project. A project will have little chance for success if the business drivers are not supported by its introduction.

**Application Driven Benefits Using Standards**

Process cycle times are being decreased and the numbers of products produced increased to match the demands for a greater number of batches and variety of products. To support these manufacturing objectives while needing improved visibility and control of the entire process, enterprise business systems are being integrated to batch managers and other plant floor systems. There are a number of design and model standards specifically created for process automation and integrating manufacturing control to business processes. Applying these standards during the implementation have yielded considerable financial benefits when applied across the plant floor.

**ISA 88**

The ISA 88.01 standard (Ref. 12) provides standard models and terminology for the design and operation of batch process control systems. It is being applied to in a number of successful projects. Application of the standard to has been used on projects at Kraft Jacobs Suchard and B.F. Goodrich (Ref. 13). S88 has been used as the design foundation for a production Quality Assurance process for a polymerization plant that involved enterprise business process integration (Ref. 14).

The design and model principles contained in ANSI/ISA S88.01 were used at Genentech’s Vacaville, CA site, (Ref. 15, 16). The implementation was a large complicated batch process for large scale, cell fermentation and recovery processes. A number of benefits were achieved by using the 88.01 concepts as the basis of the implementation including:

- Product and process flexibility was achieve using the detailed model design standards
- A higher degree of production success rate was achieved by implementing equipment tracking and product status reporting
Cycle time was reduced and product releases improved due to efficient data presentation and review as well as anomaly resolution. The implementation achieved a time saving of over 60,000 hours ($3,000,000 using a conservative effort rate of $50.00/hour) of contractor development effort for the control modules, $900,000 in unit (including phases) development and testing savings of $300,000. A total project saving of $4,200,000 was attributed to using the S88.01 model standards.

**ISA 95**

The ISA S95.01 standard provides consistent models and terminology for defining the interfaces between an enterprise’s business systems and its manufacturing control systems. The manufacturing reference model for the standard is the Purdue Reference Architecture. The activities covered by the specification are given in Figure 3. The models and terminology defined in this standard,

- Emphasize good integration practices of control systems with enterprise systems during the entire life cycle of the systems
- Can be used to improve existing integration capability of manufacturing control systems with enterprise systems, and
- Can be applied regardless of the degree of automation

Specifically, this standard provides a standard terminology and a consistent set of concepts and models for integrating control systems with enterprise systems, which will improve communications between all parties involved; and that will

- Reduce the user’s time to reach full production levels for new products;
- Enable vendors to supply appropriate tools for implementing integration of control systems to enterprise systems;
- Enable users to better identify their needs;
- Reduce the cost of automating manufacturing processes; and the

Batch management and manufacturing control applications allow engineers and operators to access, analyze, summarize, and report production data. Integrating that data through batch management to the enterprise will enable quicker and more informed decisions on running the process, produce higher yields and reduce recipe and process deviations. These types of results can be quantified into positive benefits to support the financial justification of the project.

Secondary and strategic benefits at this level are statistical process control (SPC), advanced control to optimize profitability, yield and throughput, and recipe management for batch operations.

Production control provides the distribution of relevant schedules and procedural information to distributed control systems, PLCs and work-centers. Scheduling has a big impact. A number of pharmaceutical manufacturers admit to having 30 to 60 days of WIP inventory due to scheduling and other queues for products who’s recipes or work orders containing one day of value-added labor. A finite capacity scheduler may provide significant benefits when integrated into the enterprise solution. Scheduling of constrained resources like unique worker skills, special equipment, etc. to support cGMPs is another area that can yield significant benefits.
Integrating the manufacturing resource planning (MRPII) functionality of ERP or MES into the automation program closes the loop that develops the full capabilities of the planning function. With materials costs being between 40% to 50% (and as much as 80%) of the cost of manufacturing, potential benefits can be derived from reductions and productive use of raw, work in process (WIP) and finished goods inventory. Primary, secondary and strategic benefits can be identified by integrating manufacturing execution with electronic work instruction systems to enhance the level of compliance while reducing costs of paper record systems.

A number of companies have installed MES and have presented experiences and perspectives on the costs and benefits of equipment integration, EBRS, and enterprise-wide integration (Ref. 17, 18). Increased productivity yielding positive business benefits can be achieved through the information integration of external devices to automate manufacturing functions and process monitoring systems to the operator’s workstation (Ref. 18, 19).

Pfizer, Inc. has integrated its LIMS into other business applications at a plant in Ireland (Ref. 20). The plant operates on a 24 hour by 7-day schedule with raw materials coming from many parts of the world. The system goals included integrating the quality system with existing MRP systems, allowing rapid transfer of information between the warehouse, laboratories, purchasing, shipping and accounting departments.

**Summary**

Pharmaceutical automation projects are being implemented to support enterprise wide goals, and their objectives are required to demonstrate higher rates of returns on investment expenditures. Concurrently, these projects are becoming more complex. Greater measurable economic benefits in the form of increased yields,
reduced manufacturing and order processing cycle times, manpower rationalization, and control of validation resources are being required to justify projected expenses for these new systems.

System Life Cycle methodologies using S-88 and S-95 standards are being used in system implementations across the plant floor. For regulated industries, electronic record keeping and system validation must be addressed in these new initiatives. When used as the basis for project implementations, standards like S-88 and S-95 can be related directly to benefits especially in the pharmaceutical industry where system validation is a regulatory requirement. Primary, secondary and strategic benefit sources for measurable economic benefits in each functional area of regulated and non-regulated operations have been achieved using these existing and emerging standards.

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