Understanding Validation Cost
Agenda: Understanding Validation Cost

- How to understand validation cost
- Cycle time and the impact on cost
- Capital versus ongoing operation cost
- Work force modeling
- Validation cost drivers
- Understand your current cost model
Agenda: Validation Cost Reduction

• What is Lean Validation?
• Identify validation waste
• Reduce cycle times
• Cost reduction ideas
History of the Problem
"We Are Producing Two Things: Paper And Drugs"

Look familiar ?!
Problem Statement

• COST OF VALIDATION
  • ~ 25% of the total capital

• TIME
  • Inadequate cycle times
  • Effort takes too long
  • Inability to support timelines based on business needs
What do we typically see?

- Inconsistent practices
- Moving target expectations
- Unclear roles and responsibilities
- Significant duplication of effort and rework
- Significant resource commitment
- Functionally siloed activities
- Re-interpretation of requirements leading to re-drafting of protocols
- Excessive reviews / approvals for each protocol
- Many unnecessary handoffs
What is the impact?

- Increased cost
  - Schedule delays
  - Negative business impact
- Work environment
Famous Validation Quotes

• Don’t change the system! It takes too long to validate!

• Validation is a waste of time and money!

• The FDA doesn’t care about validation! Only quality want us to validate!
Famous Validation Quotes

• Validation is too expensive!

• If the system fails is validation fault!

• If we change the terminology and don’t call it IQ/OQ/PQ we save money!

• The MTSA standard is law and will help us to reduce validation cost!
Famous Validation Quotes

• Lets take a risk based approach and don’t test the system!

• The only group qualified to validate is the technical SME?

• Who cares about commissioning? If we don’t finish validation will find our system errors
Understanding Validation Cost

- Validation Drivers
- Cycle time
- Hours per activity
- Waste = Bottlenecks
- Work force modeling
Validation Drivers

- Change control validation support
- New Product Introductions
- Capital Projects
- IT Projects
- QC Projects
Validation Cycle Time

• The period required to complete one cycle of a entire validation activity
• Reducing cycle time has a cascading effect on cost. As cycle times are reduced, productivity increases proportionally
Goal is to reduce cost without having a negative impact in quality

Goal is to reduce cost without jeopardizing the intent of the process

Cycle time reduction initiatives must include an assessment of any potential negative impact to quality and the intent of the process
Hours per Validation Task

• The period required to complete one cycle of a validation task
  • Protocol Generation = 4hrs
  • Protocol Pre-Approval = 3hrs
  • Protocol Execution = 2hrs
  • Protocol Review & Post Approval = 2hrs

• Hr’s per validation task can be obtained from a time study

• Hr’s per validation task can be obtained from historical project data
Waste

Types of Waste

WAITING
Any non-work time waiting for information, supplies, or equipment

PROCESSING
Doing more work than is necessary

INVENTORY
Maintaining excess inventory throughout all processes

CONVEYANCE
Wasted effort to transport any materials or equipment into or out of storage or between processes

CORRECTION
Repair or Rework

MOTION
Any wasted motion in picking up or placing, also wasted walking

OVERPRODUCTION
Producing more than is needed before it is needed
Resource Modeling

• Process by which the need for skilled workers at a particular point in time (demand) is matched directly with the availability and preference of skilled workers (supply).

• Mathematical models may be used to perform sensitivity analysis and generate data output in the form of reports and schedules.
Resource Modeling

- Inputs
  - Upcoming Projects
    - New Bioreactor
    - Process Control System Upgrade
  - Validation Drivers
    - System changes
    - Capital projects
    - QC projects
- # Validation Activities
  - 20 Validation Plans
  - 30 IOQ Protocols
Resource Modeling

• Inputs
  • Hrs. per validation task
    • IOQ Protocol (creation, review & approval, execution) = 50hrs
    • Validation Plan = 10hrs
Resource Modeling

- Outputs
  - Total Hours
  - # Resources Needed
  - % Activity Drivers
Interactive Exercise

• Each team identifies 3 areas for validation cost reduction
• Present current status
• Proposal for one area with the highest cost reduction potential
• 15 minutes
Validation Cost Reduction
What is Lean Validation?

- Lean Validation is defined as the delivery of validation services with as little “waste” as possible
Let’s Re-design the Process

• Integration and alignment of Qualification & Capital execution

• Application of Front-end Loading (FEL) principles
  • Early cross-functional involvement, understanding, consensus and commitment
Re-design Tools

• Defined, integrated work flow process
  • Identification of key milestones
  • identified interdependencies between construction & qualification activities

• Responsibilities Matrix
  • Defined roles and responsibilities

• Standard Qualification templates
  • Process & Packaging Equipment
  • Automation
Benefits

- One aligned, integrated, streamlined capital/qualification process
  - established documentation, testing
  - defined roles, responsibilities, accountabilities
  - standardized best practices
- Regulatory compliance
- Expedited capital execution process
- More effective planning, scheduling
- Reduced costs
- Productive work environment
Cost Savings

• Reduced cost to less than 20% of capital expenses
• Achieved a cost profile of 10% or less of capital expenses
• Eliminating or reducing non-value added work
Some Other Lean Validation Ideas
Document Approvers

• Typical approval cycle is more than five validation documents approvers

• Lean approach for document approvers should be two

• Lean Approach: Two document approvers
  • System Owner
  • Quality
Benefits (of reduced approvers)

- Reduced cycle times
- Faster turnaround
- Cost efficient
- Reduced numbers of EDM users
- Lower license cost for document approvers
Pre-Approved Verification Forms

- Implementation of verification forms instead of protocols
  - Driven by SOP
  - Forms are pre-approved with SOP
  - Installation & Functional Verification forms
  - Forms can be created by leveraging existing protocols
Pre-Approved Verification Forms (cont.)

- Forms can be created from requirements and design documents
- Forms can be used for the validation of changes to existing systems
- Examples of verification forms
  - Security verification
  - Recipe verification
  - Audit trail verification
  - Parameter verification
  - P&ID verification
  - Loop check verification
Verification Forms (cont.)

System Number: __________CC # (s) / WO #(s): __________

System(s) Description: ____________________________________________________________
Requirements document: ______

<table>
<thead>
<tr>
<th>Step</th>
<th>Action</th>
<th>Expected Response</th>
<th>Actual Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Login with Administrator account into the application.</td>
<td>Successfully logged into the Administrator account</td>
<td>Does Actual response meet the Expected response?</td>
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<td>Yes</td>
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<td>Verification Criteria:</td>
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<td>Visual</td>
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<td>Screenshot</td>
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<td>N/A</td>
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<td>Screen shot Attached:</td>
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<td></td>
<td>Yes</td>
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<td></td>
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<td>Attachment #: ______</td>
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<tr>
<td>2</td>
<td>Document the user group to be modified.</td>
<td>Appropriate user groups are identified</td>
<td>Does Actual response meet the Expected response?</td>
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<td></td>
<td>Yes</td>
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<td>Verification Criteria:</td>
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<td>Visual</td>
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<td>Screenshot</td>
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<td>N/A</td>
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<td>Screen shot Attached:</td>
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<td>Yes</td>
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<td></td>
<td></td>
<td>Attachment #: ______</td>
</tr>
<tr>
<td>3</td>
<td>List the privileges to be Added /Modified /Deleted</td>
<td>Privileges are documented</td>
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User Rights Verification

<table>
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<tr>
<th>Step</th>
<th>Action</th>
<th>Expected Response</th>
<th>Actual Response</th>
<th>Meets Acceptance Criteria (Pass / Fail)</th>
<th>Verified By Initial / Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
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</table>

Step Action Expected Response Actual Response Meets Acceptance Criteria (Pass / Fail) Verified By Initial / Date
<table>
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<tr>
<th>Step</th>
<th>Action</th>
<th>Expected Response</th>
<th>Actual Response</th>
<th>Meets Acceptance Criteria (Pass / Fail)</th>
<th>Verified By Initial / Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>7</td>
<td>Log off from the User account.</td>
<td>Successfully logged off from the User account</td>
<td>Does Actual response meet the Expected response?  Yes  No</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Verification Criteria: Visual Screenshot N/A Screen shot Attached: Yes  No. Attachment #:</td>
<td></td>
</tr>
</tbody>
</table>

Completed by: ___________________________ Date: _____________

Approved By Quality (Print/Sign): ___________________________ Date: _____________
Benefits of implementing verification forms

• Cycle time reduction
• Faster turnaround time
• Only one approval cycle
• Cost reduction: ~ $750 per form vs. $5,000 per protocol
Integrated equipment and automation verification

- Installation and functional verification forms
  - Pump verification
  - Alarm/interlock verification
  - Valve and miscellaneous equipment verification
  - Agitator verification

- Integrating equipment verification forms into the automation protocols

- Leveraging calibration data
Benefits of integrating equipment and automation verification

- Reduced number of verification documents
- Cycle time reduction
- Faster equipment turn around time
- Cost reduction
Standard Fixed Price Qualification Packages

• Background
  • Fixed Price Computer Validation

• Equipment (SIP qualification example)
  • Traditional approach cycle time is ~ 160hrs
  • Traditional approach requires a minimum of two resources for a total cycle time of ~320hrs
  • Current approach cost ~ 23K for a 15 point or less SIP PQ
Standard Fixed Price Qualification Packages (cont.)

- SIP PQ fixed price package
  - PQ Protocol Generation
  - Thermocouple Calibration
  - Placement of TC’s and BI’s
  - Execution of 3 Runs
  - Removal and Cleanup
  - Submission of BI’s
  - Discrepancies
  - Data Analysis
  - Final Report
Standard Fixed Price Qualification

Packages (cont.)

• Fixed Price SIP PQ

• Cost for 15 points of less $5,865.00 vs. $15-20K for traditional approach

• No contractor billing for “down” time on the bench

• Full time employees provide program management and oversight
SIP PQ Fixed Price Package: Efficiencies

• Significant cost reduction $5,800 vs 23K

• Predictable cost model provides cost reduction and consistency

• No SIP PQ execution by company employees
SIP PQ Fixed Price Package: Efficiencies (cont.)

- Eliminates contractor “down” time cost
- Consistent execution
- Ideal approach for SIP yearly PM program
- Lower cost for capital projects SIP PQ’s
Change Control

• Issues impacting validation cost
  • Excessive and unnecessary change record rejects
  • Excessive and unnecessary change record reverts
  • Change mis-classifications
  • Excessive amount of change assessors
  • Unnecessary gates that don’t allow parallel task execution
Change Control

• Simplifying Change Control
  • Reducing change record reverts & rejects
    • Simplify rejection & revert criteria
    • Risk based approach
  • Change mis-classifications
    • Proper classification of changes based on risk
    • Redefining classifications
    • Not driving classifications based on validation impact
Change Control

• Simplifying Change Control
  • Excessive amount of change assessors
    • Reduced number of assessors based on change impact
      • Technical SME
      • System Owner
      • Validation
      • Quality
  • Unnecessary gates that don’t allow parallel task execution
    • Break gates and allow parallel activities
    • Combine task in Trackwise for parallel execution
Assessment Tools

• How you determine the GxP and overall system impact?
  • Meetings
  • Endless debates
  • Relying on SME’s
Assessment Tools (cont.)

• Efficient Assessment tools
  • Short (cycle time hrs vs days)
  • Simple (5 pages or less)
  • Eliminates unnecessary meetings
  • Eliminate lengthy debates

• Examples Assessment Tools
  • GxP
  • Part 11
  • Risk impact (H,M,L)
Part 11 Assessment Tool

1. Once the system is considered “GMP system”, assess the Part 11 applicability using the questionnaire below.
2. If the answer to question 1 and 2 is “Yes”, Part 11 applies and answer questions for categorizing system.

<table>
<thead>
<tr>
<th>Part 11 System Categorization</th>
</tr>
</thead>
<tbody>
<tr>
<td>Step No.</td>
</tr>
<tr>
<td>Is the System an Electronic Record System (EREC)?</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>NOTE: If the answer to questions 1 and 2 is YES then continue with the Part 11 checklist.</td>
</tr>
<tr>
<td>Is this a Hybrid System?</td>
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<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>Is the System an Electronic Signature System (ESIG)?</td>
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<tr>
<td>5</td>
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<tr>
<td>6</td>
</tr>
<tr>
<td>Is the system an open system?</td>
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<tr>
<td>7</td>
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<tr>
<td>8</td>
</tr>
</tbody>
</table>

**Conclusion:** The Systems is (Enter Yes or No in each column)

<table>
<thead>
<tr>
<th>EREC</th>
<th>Hybrid Systems</th>
<th>ESIG</th>
<th>Closed</th>
<th>Open</th>
</tr>
</thead>
<tbody>
<tr>
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</table>
Paperless Validation

- Eliminates paper validation documentation and system specifications
- Integrates electronic deviations to protocols
- Enables global collaboration between sites and corporate teams
- Integrates the creation of traceability matrix with electronic protocols
- Enables electronic execution of protocol
- Electronic review and approval of protocols and system specifications
Paperless Validation

• Automates and manages the validation life cycle and
• Provides real time validation status of any system and metrics
• Expedites the validation process and removes the inefficiencies that plague paper-based processes
• Provides a holistic view of project status and validation deliverables for internal and external auditors, with real time status
Paperless Validation: Benefits

- Significant cycle time reduction
- Significant error reduction
- Enables faster release of equipment to support GMP operations
- Return of investment of less than 12 months
Paperless Validation: Vendors

- ValGenesis
- Kneat Software Validation Lifecycle Management
What is the impact?

• Lower validation cost for capital projects
  • Less than 10%
  • Faster system turnaround time
  • Improved resource utilization
  • Faster new product introduction
Summary

• During this session, we covered the following concepts:
  • Lean Validation Strategies
    • Redefining system boundaries
    • Integrating equipment and control system
    • Integrating Commissioning and Qualification Activities
    • Standard Fixed Price Qualification Packages (e.g. SIP PQ)
    • Assessment Tools
    • Paperless Validation Systems
Questions?