ASTM E2500 Lessons Learned

The Good, The Bad and The Ugly on Implementing a New Approach

Agenda

• Project Background
• Execution Strategy
• Lessons Learned
• Best Practices
Project Background

- Renovation and expansion of an existing processing suite
  - Suite was never released for production
  - Support product transfer
  - Upstream process
    - Modifications to an existing Seed and Production Bioreactor
    - New control system
    - New centrifuge and powder transfer system
    - Modifications to existing harvest tank farm
  - New media and buffer prep tank farm
    - Controls
    - New down stream process equipment
      - Chromatography columns

- Utilities
  - Modifications to USP water & WFI systems
  - New Clean Steam Generation and Distribution System
  - Expansion of plant utilities
  - New AHU for process areas
    - Control system
    - Separate Data historian and alarm

- Facility
  - New processing suites
Project Background

• Project Driver
  • Schedule
    • 7 months to complete construction, commissioning and verify equipment fit for intended use
    • 1st engineering run May 2008

Project Background

• Compliance
  • Client had good history of compliance
    • No non-compliant observations from recent FDA or customer audits
  • Sites Validation Staff had strong technical knowledge about equipment and systems
Execution Strategy

• Use an ASTM E 2500 approach to meet schedule
  • Focus efforts on making sure system/equipment meet installation and performance requirements
  • Reduce redundant testing and documentation
  • Eliminate effort on addressing “protocol deviations”
• Integrate with Construction
  • CQV team responsible for construction QA and startup activities
• Team Approach
  • Comprised of Project, and Client’s Operations, Maintenance and Validation Personnel

Execution Strategy

• Requirements Definition
  • Project URS, Batch Record and SOP’s used to develop downstream documents
    • Site Procedures allowed use of ASTM E2500
• Specification and Design
  • Critical attributes identified in specifications and drawings
    • Documentation requirements for OEM’s and Contractors
  • Design review and approval of P&ID’s, ISO’s and OEM/Contractor submittals
Execution Strategy

- Verification
  - Commissioning
    - Information and data used to verify fit for intended use.
  - Activities
    - Skid: Mechanical & Electrical Inspection, FAT,
    - Field: Progressive installation verification walk downs, Construction QA results
    - Site Acceptance Testing

- Documentation
  - Inspection reports
  - Construction QA Results & As-built Drawings
  - FAT & SAT documents
  - Commissioning protocol
    - Engineering field reports
    - Punch list
      - Record of the issues and resolutions
Execution Strategy

• Verification
  • Review
    • Progressive review of Commissioning documents
    • Final approval of document by client’s validation staff
• Acceptance and Release
  • IOQ Protocol format
    • Referenced commissioning data, system SOPs, training, and calibrations

• Verification
• Acceptance and Release
• IOQ Protocol format
  • Review of commissioning data, system SOPs, training records, and calibration data
  • Included performance testing for certain systems
  • Contained a “Release for Use” Statement
  • Approved by Client: Quality, System Owner, Validation
Lesson Learned

• The Importance of Design Review
  • Problems with existing systems and equipment
    • In-depth review to identify risks and develop mitigation plans
      • As-built inspections
      • Performance testing (water or mock runs)
      • Review of life-cycle information
  • No problems report on new equipment

Lessons Learned

• If you always do what you always did, you’ll always get what you already got.
  • Hard to get stakeholders to feel comfortable with new approach
    • Tendency to migrate to previous methods
    • Quality documentation does not make up for bad design or poor fabrication/installation
Lessons Learned

• Be a Good Consumer
  • Clearly define what the OEMs and Contractors are responsible for:
    • Design, Submittals, Quality and Acceptance Testing, and Documentation
  • Track performance
  • Do not over or under buy

Lessons Learned

• Importance of Subject Matter Experts
  • New control program for bioreactors did not meet process expectations
    • Client did not have expert to work with automation contractor
    • Approved requirements and specifications did not meet process requirements
Best Practice

• Team Approach
  • Four teams based on functional areas
    • Fermentation, Purification, Media/Buffer & Facility/Utilities
  • Responsibilities:
    • Commissioning and Verification activities for systems/equipment within area
    • Coordinating activities with construction and OEM
      • Including issue resolution

Best Practice

• Team Approach
  • Structure
    • CQV Specialist(s)
    • Engineering expert (SME/Designer)
    • Operation Representatives
    • Maintenance Representatives
  • One member of the team was the leader
    • Coordinated activities and efforts
Best Practice

- System Specific Punch Lists
  - Tool to document history
    - Progress of Installation/Fabrication
    - Installation and performance issues and resolutions identified during commissioning
    - Support life-cycle design reviews
  - Managed by the team

There is nothing wrong with change, if it is in the right direction

Winston Churchill
Thank you

Questions?

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