Introduction

• What are Retrofit Projects?
  – Upgrades / Renovations / Expansions in existing facilities
  – Concurrent with manufacturing operations or during shutdown periods.
Overview

• Key considerations for various lifecycle stages of retrofit projects
  - Design – Planning – Execution – Completion
• Illustrate with some “war stories” (audience participation encouraged!)
• Share some techniques & tools
• Q&A

Retrofit Goals

• Manufacturing:
  “When can I return to routine production?”

• Quality / Regulatory:
  “How can you prove to me there was no impact on operations?”
Design

Design Approach

• Involve key stakeholders as early in concept phase as possible:
  – Manufacturing, first and foremost
  – Facilities, QA, QC, Validation, Regulatory, HSE
• Identify likely impact areas
• Preliminary discussions of mitigation strategies
• Know what are considered to be deal-breakers
Physical Constraints

• Doorways / Ceiling heights / Floor loading
• Clearances for equipment to turn corners
• Operational accessibility
  – Is temporal segregation needed?
  – If so, added cleaning demands? Adequately supported?
  – Shipping/receiving schedules impacted?

Capacity Issues

• Utility supplies
  – Look beyond generation: Are storage & distribution sufficient for new loads & diversity?
  – Beware of cascading effects:
    • More clean steam requires more WFI requires more RO requires more incoming plant water
• Power supply
  – Adequate to maintain operations and support project demands?
  – Adequately isolated to protect ops?
  – Utility Power or Emergency Power or UPS?
Design Basis

• Question any assumptions of records reliability
  – All start-up / walk-down / commissioning changes complete and documented?
  – Beware if drawings updated on yearly basis; make sure to check red-lined versions
  – Walk down a sample of required documentation – then 100% of a class if significant errors found

• Is investigatory work required, warranted?

“Creative” Designs – Good or Bad?

• Multiple storage tanks vs. sub-loop systems
• Utilize gray space
  – GMP space savings vs. clean sampling capabilities
• Custom designed equipment
  – Challenge the custom aspects of the design during FAT

• “c”GMP / best practicable solution
• Consider CQV impacts of each approach
Acceptance Testing

• Do your FAT conditions match site conditions?
  – Quality, Volume and Flow Capacities: Steams, Purified Waters, Cooling, Air
  – Environment: Cleanliness, Temperature, Heat Removal, Humidity

• Will SAT requirements fit with ongoing manufacturing needs?
  – Beware of challenge testing impacting manufacturing operations

Risk Assessment

• For project – identify and mitigate most likely impacts to manufacturing

• Maybe more important - look back at prior assessments to determine if any safeguards will be compromised during retrofit
  – Are redundancies compromised?
Regulatory Impact

• Does retrofit work include facility modifications?

• Impact on regulatory filings? Consider:
  – Materials of construction
  – Personnel, material & product flow patterns
  – HVAC impacts (air changes, air flow patterns)

Planning
Calibration/PM Survey

• As-found data collection prior to start
• Don’t forget to take advantage of opportunity for Calibration/PM work
  – What operating units are coming due during retrofit? Verify that calibration/PM needs can be met
  – Look for opportunities to pull in events in retrofit area to avoid a second interruption
• Beware PM tasks overstressing systems already taxed by supporting both operations and retrofit
  – Plan ahead and staff up as required

Environmental Protection

• Verify gowning requirements for retrofit space
• Bag-in / bag-out for traversing active space
• Enhanced cleaning requirements
  – Contractor responsibilities
  – Routine cleaners responsibilities
  – Manufacturing responsibilities
• The regulatory/QA perspective: how to verify environment unaffected by retrofit work?
HVAC Issues

• If temporary barriers to be use, determine impact on air changes / air flow profiles
  – Will work necessitate segregation of supplies from returns? If so, how will you verify no impact to operation?
    • Consider enhanced sampling / monitoring

• Will project work require replacement of HEPAs at completion?
  – Certification and qualification requirements
  – Contingency spares

Resources

• Internal departmental support
  – QC: sampling & testing
  – Facilities / Metrology / Cleaning Staff
  – Training for trades and contingent staff
  – QA and Validation: commissioning and qualification

• Contractor support: lead time
  – Vendor Qualification → RFQ → PO Approval → Training
  – Training on all daily permitting reporting requirements

• Supplies
  – Gowning
  – Cleaning
  – Production consumables
Return to Service Plan

• Not just a matter of completing the mechanical work
• Proactively plan:
  – Preparation of TOPs concurrent with construction
  – Handoffs: Construction -> Commissioning -> Validation -> Manufacturing – for each system
  – Release of utilities to support CQV schedule
  – Ramp up Commissioning while Construction ramps down
  – Technical Support of CQV activities:
    • Training of Facilities / Maint / Mfg on new equipment
    • Keep Trades available through commissioning: things break, flaws discovered, adjustments are required

Expect the Unexpected

• Use cross-functional team to populate a Risk Register identifying ‘pinch points’ – factors with high potential impact to the critical path
  – Manufacturing doesn’t finish on time
  – Equipment is not available or found in unexpected condition – deviation investigation, out of calibration, etc.
  – Surprises in the walls
  – State and local inspections issues
• Feed results into Risk Analysis for mitigation
Execution

Protecting Operations – The Obvious

• Performance
  – What does “Work Clean” mean?

• Logistics
  – Signage
  – Contractor parking, trailers, lavatories, access to workspace
  – Are normal flow paths maintainable? Temporal segregation? Associated cleaning requirements?

• Manpower
  – temporary support if insufficient personnel for both retrofit and routine operations
The Not-So-Obvious

• Enhanced monitoring/sampling requirements
  – EM sampling and QC lab capacity

• Vibration / Noise
  – Construction (trenching, etc.) / Equipment movement

• Electrical Isolation

• Utility support – both GMP and non-GMP
  – Which routine operations in those areas will be affected?
  – Will temporary procedures or supplies be needed?
  – Cascading release: can WFI or CS start qualification while RO is conditionally released or only after full incubation period? When can each utility be used for manufacturing?

Keeping a Manufacturing Focus

• How will project plan be communicated?
  – Manufacturing approval of / access to an up-to-date detailed schedule

• Orient thinking along the lines of how to minimize / eliminate manufacturing impact
  – Absolutely critical to have 24/7 access to decision makers from Manufacturing / QA / Regulatory

• Develop a methodology for how changes to the project plan will be communicated
Useful Tool – Work Request Form

• Thursday AM look-ahead for following week.
  – Work breakdown by area & major tasks
  – Utility impacts
  – Special requirements (hot work, etc.)
  – Contractors involved with contact info
• Friday noon sign-off by PM, QA, Mfg
  – No work without signatures

Bumps in the Road

• Non-routine use of systems creating upsets
  – Excessive flow, increased/decreased velocities, spikes
• Biofilm flaking from drying out
• Opportunity for visual inspection may have unintended consequences
  – What if you find rouge?
• Many shutdowns over December holidays – beware of idle systems freezing
• Floor repair / interference with operations
• Damage from Project Activities
Completion

Defining “Done” – Completion Requirements

Greenfield Projects:
- Mechanical Work
- Validation Reports

Greenfield Projects: TOPs
- As-Built Drawings

Retrofit Projects - all the above, and as an added bonus:
- Action Notices
- Change Controls

Retrofit Projects - Work Orders
- Regulatory Filings
Returning to Service

• Quality requirements (Waters, CS, EM, HEPA)
  – Sampling / Testing / Release
  – Contingency for failed samples

• How will documentation changes be handled if manufacturing SOPs are affected?
  – How will training be accomplished for the return to service? Make sure to include this in the plan.
**Key Takeaways**

1. Access to the team of decision makers
2. Resourcing for added activities
   - PM / Metrology
   - Cleaning
   - Monitoring/Sampling
   - Commissioning/Qualification/Validation (supported by mfg / eng / quality)
3. Detailed plan for return to service
   - Agree contingency plans in advance
Questions?

- Please feel invited to contact me

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