
# 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:

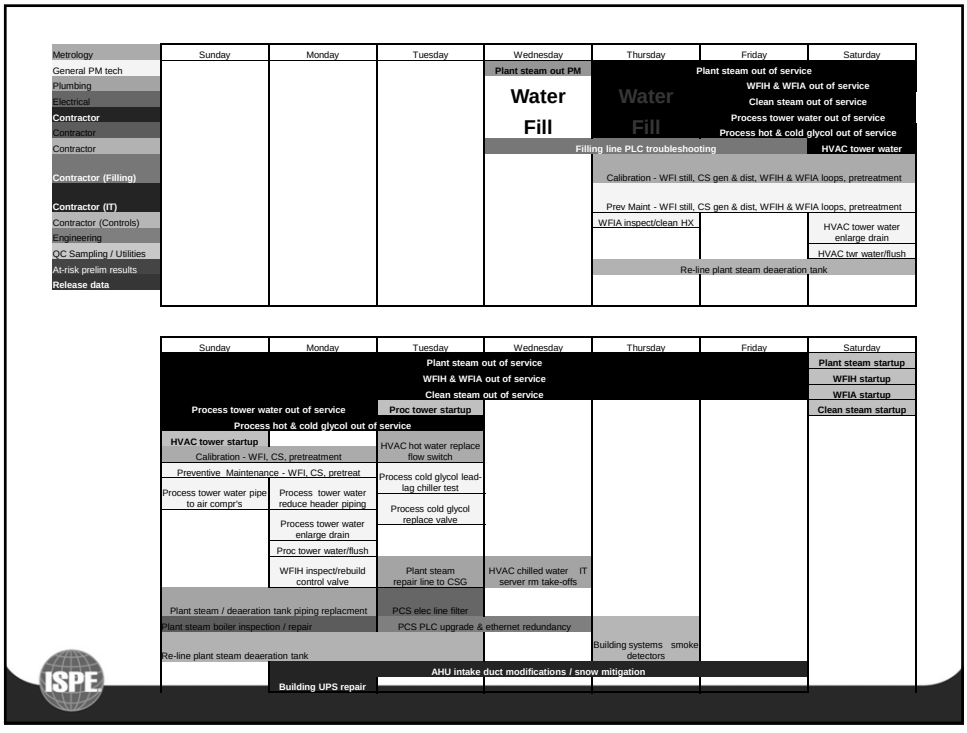
| | |
|---|---|
| Mechanical Work | TOPs |
| Validation Reports | As-Built Drawings |

Retrofit Projects - all the above, and as an added bonus:

| | |
|---|---|
| Action Notices | Work Orders |
| Change Controls | 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.



| Metrology | Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
|---|---|---|---|---|---|---|---|
| General PM tech | Sample clean steam #1 | Sample clean steam #2 | Sample clean steam #3 | | Clean steam prelim rel | | |
| Plumbing | Sample WFIH day 1 | Sample WFIH day 2 | Sample WFIH day 3 | | WFIH prelim release | | |
| Electrical | Sample WFIA day 1 | Sample WFIA day 2 | Sample WFIA day 3 | | WFIA prelim release | | |
| **Contractor** | | | | | | | |
| Contractor | | | | | | | |
| Contractor | | | | | | | |
| **Contractor (Filling)** | | | | | | | |
| **Contractor (IT)** | | | | | | | |
| Contractor (Controls) | | | | | | | |
| Engineering | | | | | | | |
| QC Sampling / Utilities | | | | | | | |
| At-risk prelim results | | | | | | | |
| **Release data** | | | | | | | |

| Sunday | Monday | Tuesday | Wednesday | Thursday | Friday | Saturday |
|---|---|---|---|---|---|---|
| | **Clean steam full rel** | | **Fill** | | | |
| | **WFIH full release** | | | | | |
| | **WFIA full release** | | | | | |

# 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

Rick Kotosky, P.E.
Integrated Process Technologies, Inc.
rkotosky@intprotech.com