

Strategies in Updating an Aging Pilot Plant Facility

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Facility & Project Background

- Started in 2000 – first clinical lot: HPV
- Capabilities for
 - Sterile and Non-Sterile Banks, Drug Substance, and Intermediates
 - BSL-2
 - Live virus
 - Multi-product
 - Solvents/Flammables
 - Potent compounds
 - Ph1-3 GMP
 - Scales up to 2000L
 - Stainless and single-use equipment
 - Consumables and RCM support areas



B17 identified design gaps against regulatory expectations for a Ph3 clinical vaccines facility. This was accomplished through:

1. Reviewing observations from Merck clinical and commercial facilities during recent regulatory inspections (FDA & MPA)
2. Compiling feedback from CMOs and other members of industry
3. Comparing B17 against Merck internal requirements and standards

BPP committed to addressing the identified gaps by:

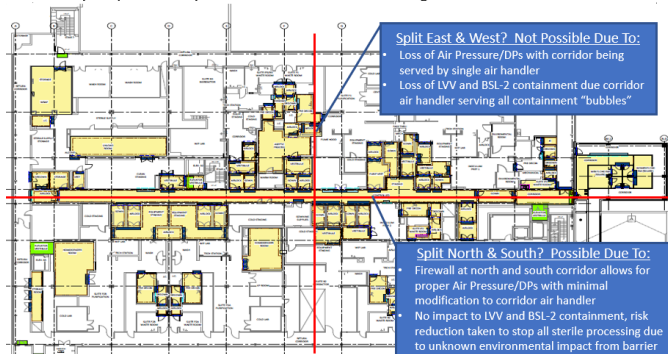
1. Ensuring proper transitions between graded spaces
2. Separating currently shared entrances/exits into graded spaces
3. Implementing proper people and material/equipment segregation
4. Addressing the lack of a locker room that exits directly to classified space on the 2nd floor

Key Assumptions

- B17 is the primary vaccine manufacturing building in the Merck network and is the long-term site for vaccine clinical manufacturing
- Pending FDA and MPA inspections will focus on facility design requirements
- Renovation work will occur in four phases. Active campaign work in BPP suites will be conducted concurrent with construction during two of the four phases.
- A Quality Risk Assessment of the proposed phased construction sequencing will be conducted, reviewed, and approved prior to start of construction activities.

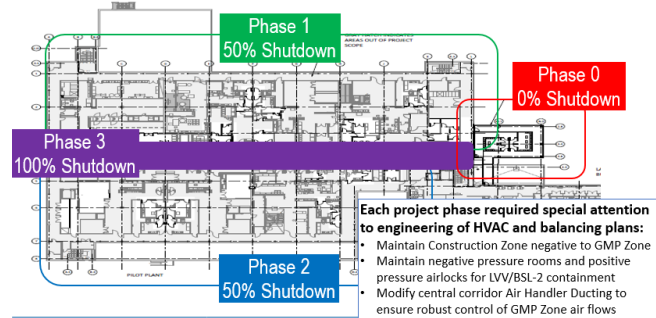
Problem statement – Maintain Operations

How do you split a facility to maintain GMP Manufacturing with Simultaneous Construction?

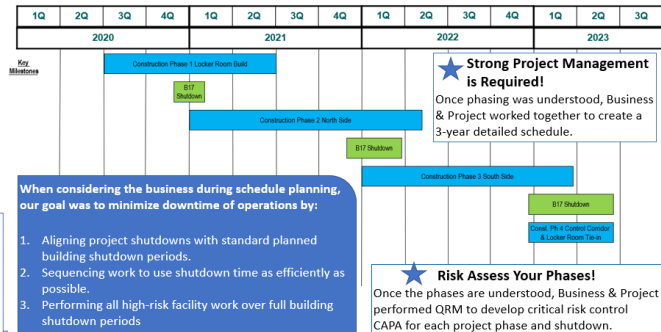


Project Phasing Strategy

Phasing Project – Construction Perspective



Phasing Project – Business Perspective



Lessons Learned

Strong Team Communication Leads to Success!



Align the right people to the right assignments

1. Project & Business - Communication Fluidity (weekly update meeting, weekly project walkthrough, weekly touchpoint meeting, tier meetings, etc.)
2. Business - Capital Lead vs Business Lead Partnership (strong partnership to negotiate between capital and operational needs)
3. Business - "Tear Down Build Up" Sub-team (comprised of all Pilot Plant functional areas and responsible for tasks entering and exiting construction, allowed for better change management within department)
4. Business - Strong Cross-Organizational Partnership (Quality Engineering, Environmental Monitoring, Quality Systems, Quality Disposition, Maintenance & Utilities, Site Engineering Services, all areas required to execute, review, or approve modifications to facilities, utilities, equipment, and documentation)

Barrier Selection Is Critical!



Future Proofing Facility

Suite access during the project was unprecedented!

Facility downtime was utilized to support multiple equipment and utility upgrades, modifications, and full replacements.

Projects Coordinated in Conjunction with Facility Project	
Sterile Supply Dry Heat Oven Removal and Creation of New Storage Footprint	Vestibule
Suite Decontamination Autoclaves Controller Upgrades	
Removal of Aging Stainless-Steel Bioreactors and Fixed Tanks	
Automation Room Relocation (No Longer in Environmentally Classified Room)	
Aseptic Isolator Purchase and Installation; OEB Isolator room prep & scoping	
Utility Panels Modified to Support Future Operations and Equipment	
Biosafety Cabinet Replacement to Updated Technology	
Suite Temperature Control Rooms Upgraded Controllers and HMIs	Processing Suite
Highly Potent Compound Modified Facility Controls	



Conclusion

- Exited each construction phase on time
 - Controlled costs under budget
 - Supported the vaccines pipeline
 - Responded to COVID issues
 - Phased project schedule allowed for agility when new vaccines entered pipeline
 - Strong team communications allowed agility in response to newly enforced safety protocols (e.g., full separation of project & business employees, lower worker density within construction areas, etc.)
 - Project Planning based on risk allowed long-lead items to be ordered early preventing delays due to supply chain issues
- Strong communications and resilient teams lead to predictive risk control and agility to respond rapidly when faced with new problems.**

