Leveraging Prefabricated Solutions to Reduce Risk

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#PDA

Agenda

- What are Prefabricated Solutions
  - How do the differ from alternate solutions
- Quality
  - Cost vs Schedule vs Quality
  - Center of Excellence
- Design Improvements
- Decon Case Study

What's the Main Difference to the Traditional Built ?

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IT'S TIME TO **SIMPLIFY CLEANROOM PURCHASES**

INNOVATIVE

RELIABLE | FULLY FUNCTIONAL | REPEATABLE | MASS PRODUCED | REPURPOSABLE | FAST DELIVERY

VS.

VARIABLE | INDEFINITE | EVERY TIME NEW | INDIVIDUALIZED | SUNK ASSET | REINVENTED AND DELIVERED

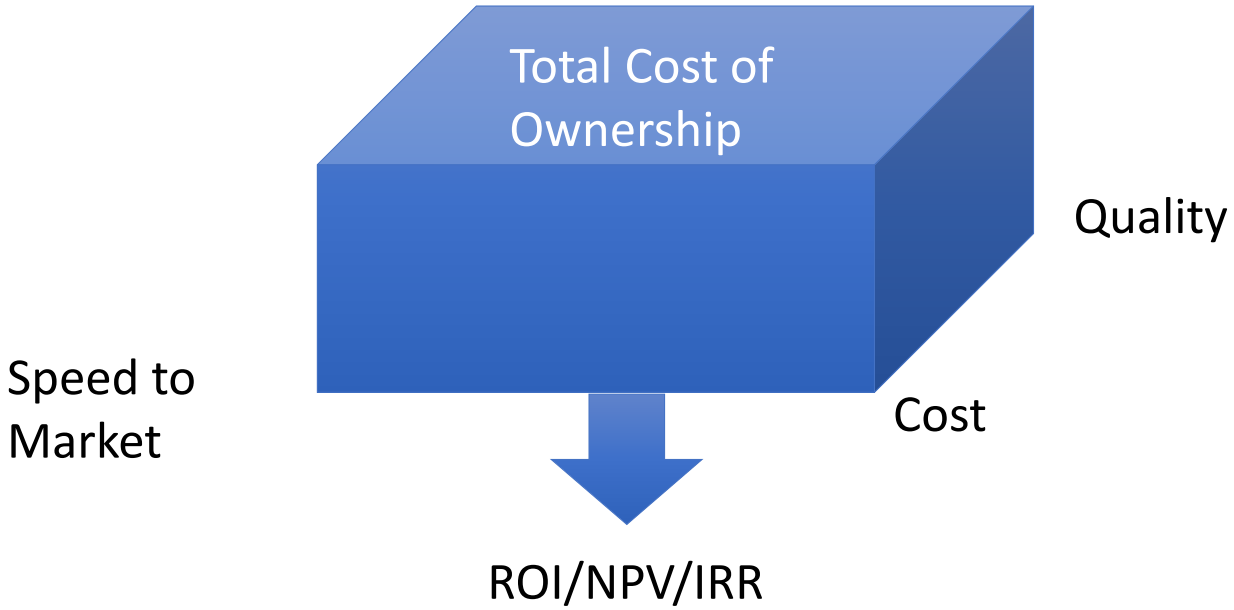
TRADITIONAL

Facility Needs Voiced

- Delivery time and budget proposals for facilities and cleanrooms require to be robust

Industry Needs

Requirements for New Facilities



Impact of Center of Excellence

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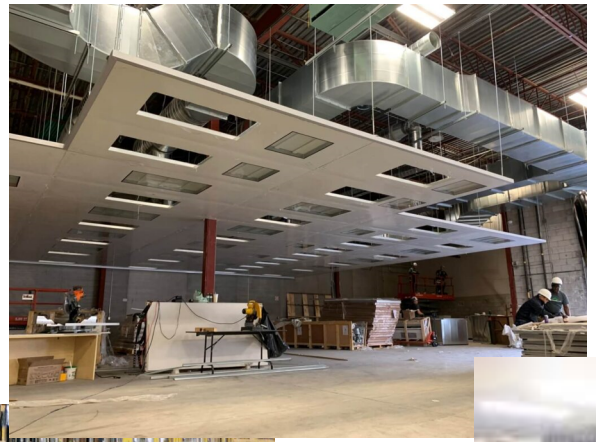
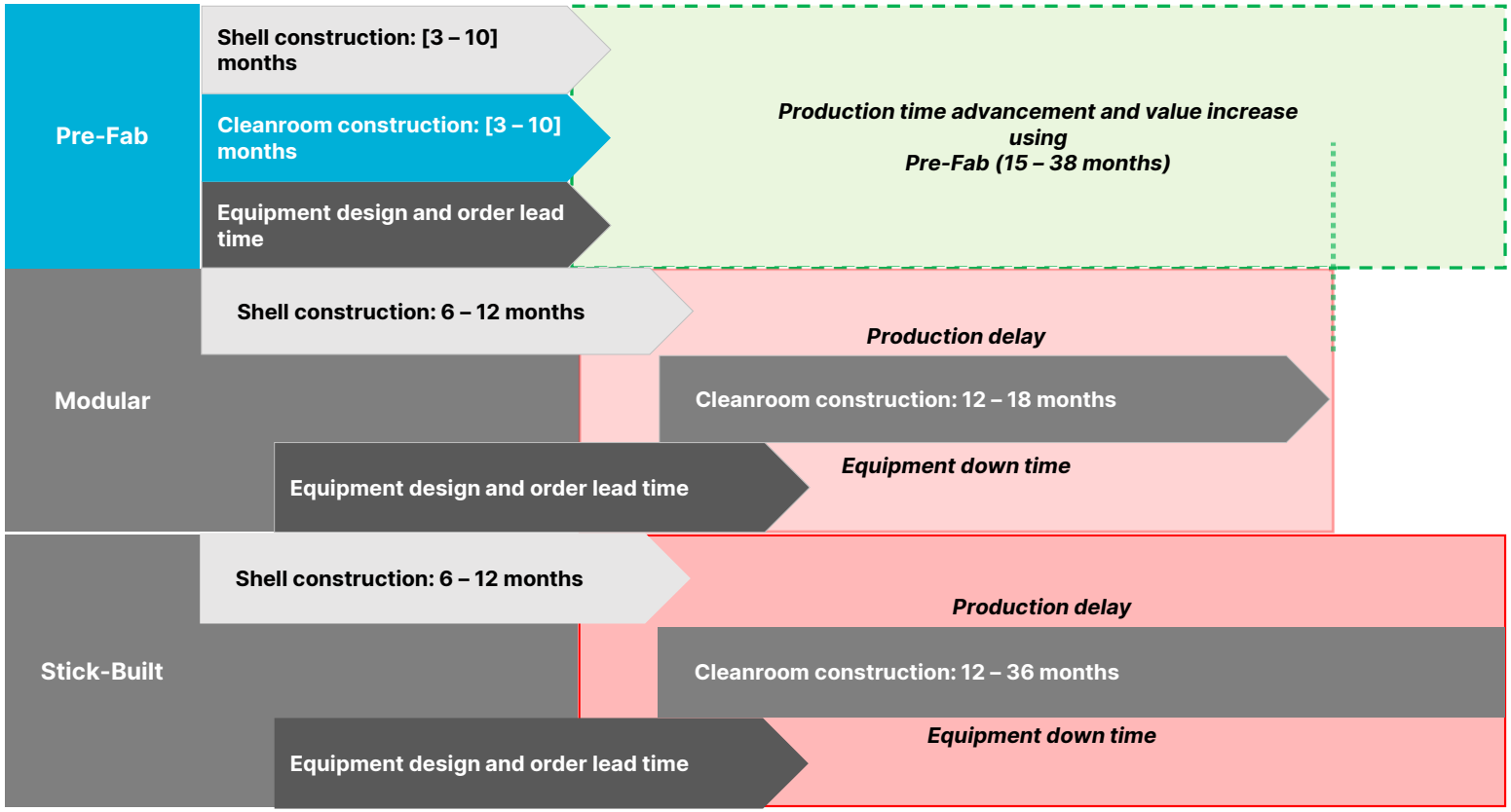


Pre-Fab Solutions– Reliable Speed

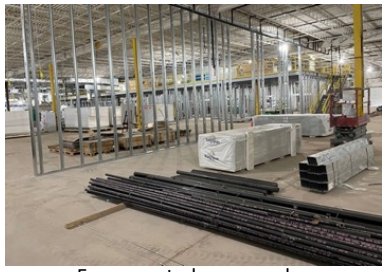


The Current Experiences in Design/Build Improvements

Experiences from the Aging Facility Task Force

- Living in the legacy mode → change averse, fear for the unknown, we have always done it that way
- Financial misconceptions → lack of total cost ownership analysis
- Let's wait → rather be a fast second than a leader
- Risk of change → do regulatory authorities accept it, is it supported by management


Human interventions

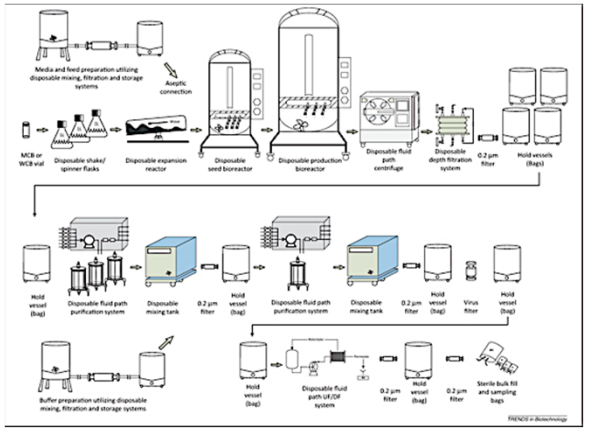

Epoxy coated gypsum cleanrooms


Stainless steel surfaces

All represent an inherent Risk by utilizing obsolete Technologies or Methods

Equipment Design Evolution

From large scale stainless steel to medium volume single-use to entire single-use process assemblies



- ✓ Higher cell densities and expression rates allowed to utilize lower bioreactor volumes
- ✓ The lower volumes and process intensification resulted in the adoption of single-use process technologies (it though took 20 years !)
- ✓ Single-use process technologies can be designed as presterilized closed systems and do not require lengthy set-up and cleaning times
- ✓ The process equipment designs are still evolving as new therapies (C/GT) enter the clinical and approval phases. The currently manual processes require a high level of automation and controls

Equipment Design Evolution, cont.

From high human intervention filling to isolator/RABS to isobots

Highest — Human Interventions — None

- ✓ Humans are a key contributor of microbial contaminations, therefore keeping the operator out of the critical area is desirable
- ✓ Isolator technology represents a great improvement, but still does not meet an optimal solution
- ✓ Isobots, contained human less environments, which utilize robotic technologies have been part of the highly critical semiconductor industry for years
- ✓ This technology started entering with robotic filling systems and move away from vials/min to output/year

Facility Design Improvements

From on-site to off-site, from putting bits and pieces put together to a prequalified, high containment units


vs.


vs.


- ✓ Off-site, prefabrication eliminates facility disruptions and break-down (no dust/construction contaminants)
- ✓ There are typically no mezzanine levels and convoluted duct systems needed, as the air handling and duct work is compact built within the technical area and plenum section
- ✓ The materials and installation used do not allow or minimize microbial contamination
- ✓ Individual areas can be shut-down and isolated in case of an excursion, sanitized without interrupting other cleanroom areas (autonomous cleanroom unit operations)

Integration of Decon

- Typically considered for BSL 2+ applications.
- Options to consider
  - VHP vs iHP vs ClO2
  - Integrated Piping vs Integrated HVAC vs Roll In Units

Evaluation of Decon Strategy

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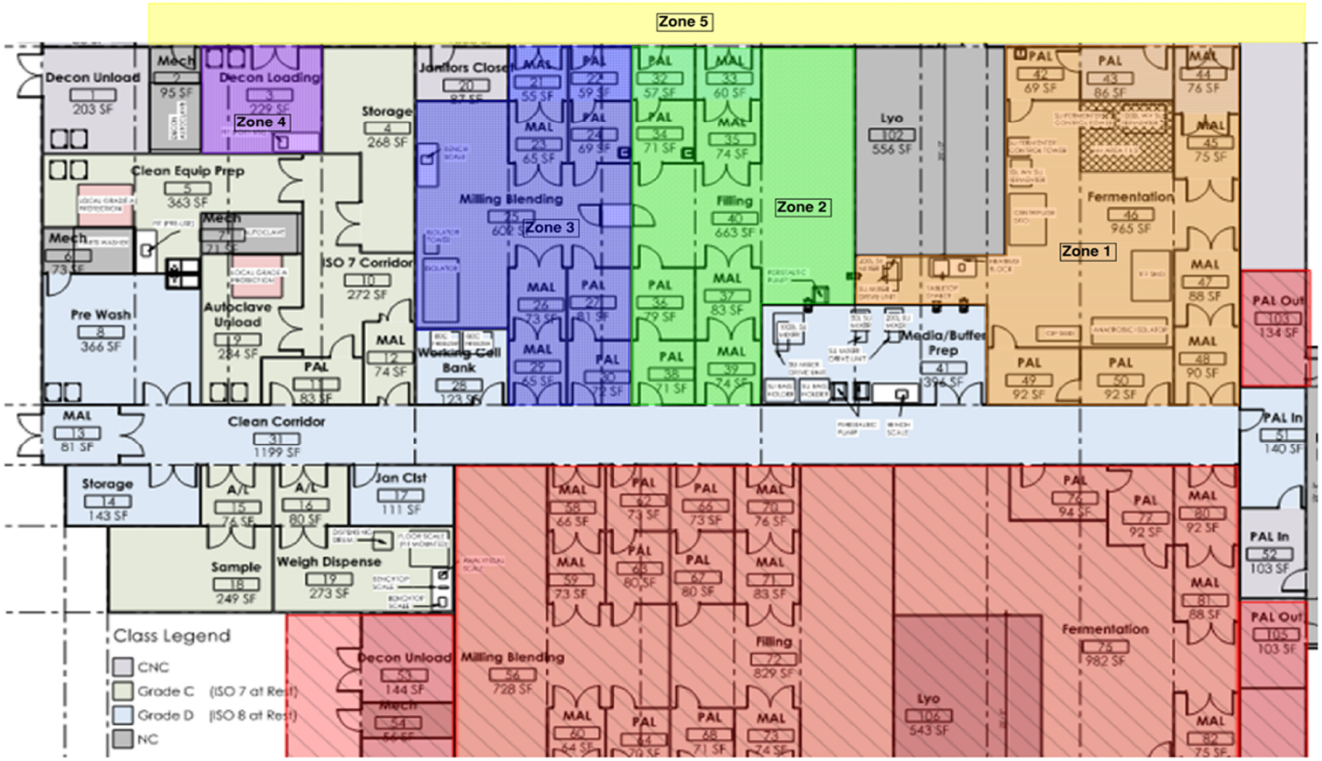
Enclosure	Volume m³	VHP concentration ppm	Injection time min.	Cycle time hours
Pass through	~1	600-1,800	10-30	0.25-1
Small isolator	~2	600-900	30-60	2-12
Small room	~30	400-700	30-60	2-12
Large room	~200	200-500	90	4-12
Very large room	200- 800	200-400	120-240	5-12



Zone Volume (10' Ceilings):
Zone 1: 16,330 ft3
Zone 2: 12,320 ft3
Zone 3: 11,410 ft3
Zone 4: 2,290 ft3
Zone 5: TBD ft3

Evaluating the Options

Decision Parameter	Portable	Integrated – HVAC Not Viable Due to Single-Pass HVAC	Integrated - Piped
Recommended Frequency of Use	Low (1x per month)	High (2-4x per month)	High (2-4x per month)
Initial Planning	Moderate	Detailed (Integration with HVAC components)	Detailed (Integration with HVAC components)
Initial Cost	$	$$	$$$
Operating Cost	$$$	$	$
Process Validation	Difficult (Manual Setup)	Easier (Fully Automated)	Easier (Fully Automated)
Operational Flexibility	High - Units can be moved between rooms and buildings	Moderate - More upfront planning	Moderate - More upfront planning
Cycle Time	2-4x longer than Integrated	Rapid (7-16 hrs for 20k ft^3)	Rapid (7-16 hrs for 20k ft^3)
Room Size Capacity	Up to 20,000 ft^3	Up to 40,000 ft^3	Up to 40,000 ft^3
Estimated Equipment Cost	$148,088 (Two Portable Units and Fans)	$350,000	$800,000 (Includes Piping)
Operator Safety	Moderate - Relying on SOP's	High - System can communicate with door interlocks	High - System can communicate with door interlocks

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DECISION PARAMETER	MOBILE VHP SYSTEM	INTEGRATED – PIPED VHP SYSTEM	INTEGRATED – HVAC
Recommended Frequency of Use	Low (1x per month)	High (2-4x per month)	High (2-4x per month)
Initial Planning	Moderate	Detailed (Integration with HVAC components)	Detailed (Integration with HVAC components)
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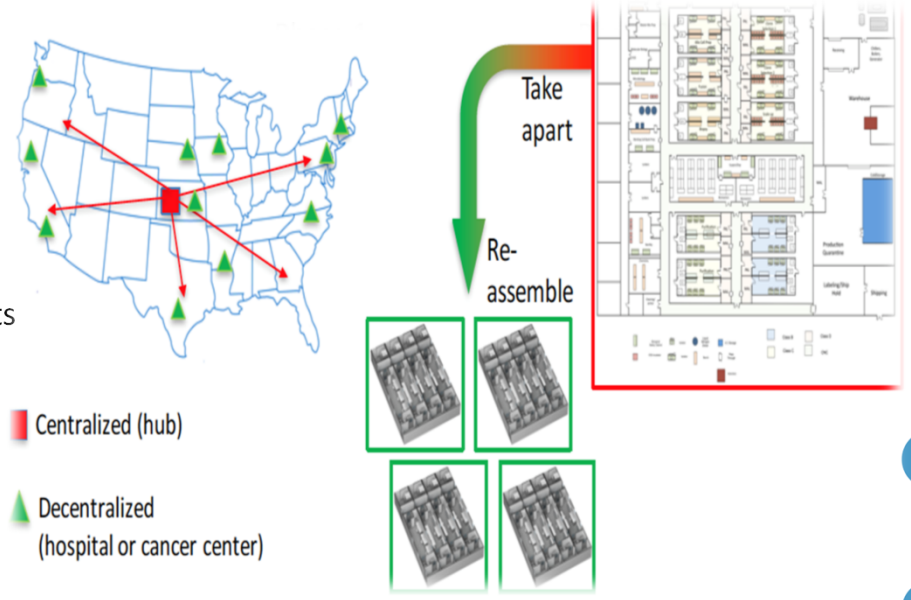
Estimated Cost Variance	$ (-)*	~ $ 1,500,000	~ $ 3,500,000

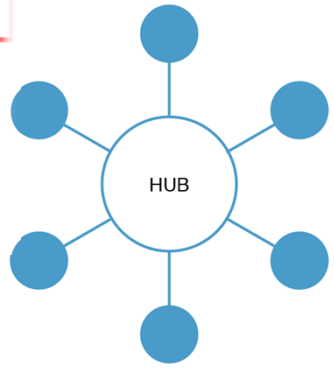
OPTIONAL ADDERS	UNIT COST
Hermetically Sealed Doors	$ 16,000 per leaf

Agile Manufacturing – Enhancing Flexibility and Scalability

- Capacity increase and scalability without interrupting existing processes

- Facilities must be able to ramp-up quickly if drug demand increases, and just as easily ramp-down if the demand diminishes
- Pre-Fab Solutions allow processes to adjust to demand
- Existing manufacturing can run, even when new units are moved into place for scale-up
- Opportunity to delay time to investment
- Redistribution or Replacement of Assets
- Allow for central core area, hub with flexible, mobile spokes





Conclusions

- Prefabricated Solutions provide a means to securing project drivers while maintaining a high level of quality.
- Execution strategy of pre-fab solutions allows for a higher level of integration with advanced manufacturing solutions.
- By nature, low end solutions such as gypsum board, are incompatible with pre-fab solutions
- Supports shut down or removal of non-compliant areas as well as facilitating an agile manufacturing network