FEXIBILITY AS DESIGN CONCEPT

Introduction to the new generation flexible, modular facilities by KeyPlants®

Jan Lilja, KeyPlants AB
80% of all conventional construction projects are delayed more than 4 months

Source: Industry Best Practise
Construction Industry Institute (CII) USA
www.construction-institute.org
Problems: Conventional Execution

- Inefficient utilization of the facility area lay-out increase construction/operation cost (HVAC etc)
- Control of many suppliers and sub-contractors is time consuming
- Escalation (change orders 10 – 15% of conventional project cost)
- A typical cost escalation of a project is + 15 - 50%, schedule slip additional 3 – 6 months
- Quality (workmanship varies with installations companies and market)
Benefits from Modular construction

-Predictability

(comparison on one project of Stick-built versus modular: for cost, schedule, quality, and productivity)

<table>
<thead>
<tr>
<th>Compliance to plan:</th>
<th>Cost</th>
<th>Schedule (1)</th>
<th>Quality</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stick-built (2)</td>
<td>+15 to 50%</td>
<td>+3 to 6 months</td>
<td>Site dependent</td>
</tr>
<tr>
<td>Modular</td>
<td>+5 to 10%</td>
<td>+1 to 2 months</td>
<td>Predictable</td>
</tr>
</tbody>
</table>

Note:  
(1) Does not account for the schedule gains (6 to 10 months) with respect to the Stick-built delivery.  
(2) Data based on large Biotech Facility; Site conditions productivity, rework...  
1 Hr in a shop requires 4 hrs in the field
Outdoor or ...

Indoor modules

Four weeks on site!
Project Execution Model

Project Funding and Approval Model

- **Project Definition**
- **Conceptual Design**
- **Preliminary Design**
- **Detailed Design**
- **Procurement/CM**
- **C & Q Site**

- **Decision Gate I**
- **Decision Gate II**
- **Decision Gate III**
- **Decision Gate IV**

**KeyPlants Design Review**

- Client Approval of BE
- BE Study Proposal
- BE Contract

**Design Review**

- Fixed Price & Schedule Design & Execution Package, C&Q Package
- Design & Execution Package

**Price Estimate +/- 25% Lay-out Design & Execution Package**

- Expected 10-15% COs from this point.
- Client risk mitigation at funding

**Fixed Price after 60-70% of DD**

- Fixed Price after Basic Engineering

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Modular Project Execution

Site Assembly, Qualification & Start-up

Transport
Modular Assembly at Site

The Genentech Example
Enhanced financial performance

- **Enhanced Cash Flow**
  Enhances cash flow due to shorter implementation schedule

- **Higher Project Net Present Value**
  Increases net present value of the investment in real terms

\[
\text{NPV} = -3 + \frac{20}{1 + R}
\]

This significantly raises the **NET PRESENT VALUE**
Risk Mitigation

- 3D modular design, process design and execution experience
- Faster and predictable execution
- Fixed price offering after Basic Engineering
- Pre-IQ and pre-testing
- Movable asset
- Off site construction in ISO 9001 certified factory
- Standardized, pre-engineered platforms
The Flexible MBS™ Platform

Complete building with fixed installations, process equipment and clean utility generation.

Optimized flexibility by allowing easy re-configuration

Scalable capacity, 500, 1 000 to X * 2 000 L SUB:s
The Flexible MAS™ Platform

Complete building with fixed installations, process equipment and clean utility generation.

RABS
Container: 2-20 ml vials
Capacity: 100/min 10 ml vials

Isolator
Capacity: 200/min 10 ml vials

PFS
Capacity: 0.5 – 10 ml
Capacity: 200/min 1 ml

All these platforms can be modified to fit the required capacity.
Flexibility – Single use or SS

Independent of any vendor or process – gives the client flexibility to stay with current vendor or possibilities to negotiate best price

100 % single-use → 100 % stainless steel

Overall design with maximized use of single-use equipment → 100 %
Flexibility - Level of Segregation

- Flexibility to match Risk Assessment

Eudralex Vol.4 (updated Jan 2014)

- Multiple air handling zones cover different process areas

- Segregated pre- and post virus removal steps

- Maximize use of closed processes and unit operations
  - Grade D

- Processing areas separated to avoid contamination
  - Grade C

- Use of laminar flow biosafety cabinets

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Additions of A/L Segregation walls

Most Appropriate 'Minimisation and Containment' Solution
- Containment Isolators in conventional area
- Dedicated suite (controlled dedicated access, HVAC, and technical area)

Increasing Probability of Occurrence

Increasing Severity (Intrinsic Physiological and Biological API Properties)

Normal multi-product facility with campaigning

Dedicated Building

Increasing Probability of Occurrence (product and process factory)

Courtesey: EFPIA, TG dedicated facilities, 2006
Flexibility – Full Integration

A fully integrated facility through easy expansion and connections according to needs – a hybrid

- Add on for MAS (Modular Aseptic Solutions™)
- Add on for Utilities
- Connection to Conventionally Constructed Warehouse
- Connection to Conventional Laboratory
- Connection to Conventional Administration
Flexibility - Relocation of Facility

1. Disassembly at first site
2. New site in preparation during disassembly
3. Reassembly at new site
4. Facility in operation at new site
5. Move it again?, same site
Flexible Scope

- The standard covers the manufacturing process from seed cultivation, harvest, purification to filled bulk in cold storage (optional MAS aseptic filling).
- Building Management System and the support functions such as washing and sterilization, weigh and dispense, in process control and disposable waste.
- Mechanical installations on level 2.
- Green Design incorporated.
Accelerated Schedule, Overlapping

1. Detail Engineering
2. Building Permit
3. Procurement
4. Modular Fabrication
5. Installation of Process Systems
6. Pre-testing
7. Transport of Modules
8. Modular Assembly and Installation
9. Commissioning & Qualification
10. Hand Over

MONTH

1  2  3  4  5  6  7  8  9  10  11  12

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CONCEPTUAL LAYOUTS

1. Microbial Vaccines MV
2. Therapeutic Proteins TP
3. Live Viral Vaccines LVV, BSL3 containment
4. CMO Multipurpose
1. MICROBIAL VACCINE, MV

Conceptual Layout
Configurations MV

Following minor configurations to the pre-engineered flexible platform Modular Bio Solutions™ have been made:

- CIP/SIP added since there are stainless steel process components
- Column packing area added
- Storage added
2. THERAPEUTIC PROTEINS, TP

Conceptual Layout
Configurations TP

Following minor configurations of the pre-engineered design with Modular Bio Solutions™ have been made:

- Increased Media and Buffer prep/hold area
- Increased Cultivation and Initial purification area
- The addition of CIP/SIP, Column Packing and Cold Storage as for the process MV
3. LIVE VIRAL VACCINE, LVV

Conceptual Layout
Configurations LVV

Minor configurations of the pre-engineered design Modular Bio Solutions™ have been made:

- Increased the level of segregation to meet the requirements of BSL3 and handling of Live Virus by adding airlocks into the live area.
- The area also includes a Virus seed lab in Grade C disposable.
4. CMO MULTIPURPOSE

Conceptual Layout
Configurations MP

Following configurations of the pre engineered design in Modular Bio Solutions™ have been made:

- Due to limited area on site a CMO requested a two storey configuration based on the MBS platform
- Only disposables (as in the original design)
- No segregation between cultivation and initial purification
- Through the floor segregation to final purification
- Buffer/Media carts by elevator to Buffer/Media hold.
Why Modular Platforms?

- Schedule within one year – shorter time to market
- Improved flexibility to produce several vaccines
- Enhanced value with integrated design and construction capability
- Subject Matter Experts in Aseptic and Biotech Processing
- Higher quality with off-site fabrication workshop ISO 9001 and OHSAS 18001 certified, with only specialized labour for all disciplines
- 3D modeling for efficient client and discipline coordination
- Standard business model to offer fixed price (ex works) after completed and accepted Basic Engineering
- Standard flexible platform concepts for shorter implementation at reduced cost
  - Cost of operations reduced through savings in labor, QA cost, validation, maintenance, utility and energy

WHAT WE GIVE (INVESTMENT)

WHAT WE GET (RETURN)

COSTS

BENEFITS

ROI (WORTH)
KeyPlants Globally

Global capabilities in Life Sciences and Process Manufacturing Industries

Part of Telstar/Azbil Group with > 2 Billion Euro in turnover and 9 000 employees whereof + 900 pharma specialists
Our Services

Our Services

- Conceptual Design
- Basic Engineering
- Detailed Engineering and Execution
- EPCM contracts
- Turn-Key Delivery
- Consultancy (Feasibility studies etc.)

Project Types

- Green field/Brown field
- Upgrades, Expansions and Renovations

Standard Facilities

- MAS (Modular Aseptic Solutions)
- MBS (Modular Bio Solutions)

Complete Range of Modular Solutions

- Building Modules
- Indoor Modules
- Process Modules/Super Skids
Acknowledgements

Vaccines
• A. Pralong

Eli Lilly
• W. Fox

KeyPlants AB
• F. Eneqvist
• A. Sjödin
• Å. Gaasvik

BioProcess Technology Consultants
• H. Levine

Contact:
Azbil Telstar, India
• Ankit Phutela, aphutela@telstar.eu
  +91-9052000824
• Sanjay Gupta, sgupta@telstar.eu

KeyPlants AB
• Jan Lilja, jan.lilja@keyplants.com
KeyPlants’ & Big Pharma

Experience with Big Pharma:

- Over 20 years on average of working biotech and pharma projects for the big 30