Project Scale-up: Lab to Industrial Plant Implementation

Prepared For:
4th Annual Next Generation Bio-based Chemicals

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Presentation

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January 28, 2013
Prepared For:
4th Annual Next Generation Bio-based Chemicals
Del Mar, California

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Process scale-up is the means by which innovations in the chemical industry are put into place in industrial facilities

- The vast majority of innovations in the chemical process industries are developed at laboratory scale at sizes better suited for careful measurement than for commercial operation.

- Implementing these advances to industrially relevant scales requires extensive investigation to ensure that unexpected problems do not scuttle a project or necessitate costly changes if they are not sufficiently anticipated in the lab.

- A new process or change in part of a process has undergone successful scale-up if:
  - A commercial size unit or plant has undergone successful startup and operation
  - The new unit or plant produces product within expectations of quality, rate and yield
  - The new unit or plant produces product near expected manufacturing cost

- A scale-up study involves attempts to replicate a laboratory process at successively larger stages in order to develop expectations of performance and a set of best practices for the ultimate industrial facility.
Introduction

There are several generally known stages for a scale-up study

All stages are not necessarily required
### There are five classical approaches to a scale-up study

<table>
<thead>
<tr>
<th>Approach</th>
<th>Cost</th>
<th>Scope</th>
<th>Scale-Up Ratio</th>
<th>Special Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full-Scale Testing</td>
<td>Low</td>
<td>N/A</td>
<td>Very High</td>
<td>Existing facilities; similar process</td>
</tr>
<tr>
<td>Modular Scale-Up</td>
<td>Low</td>
<td>Limited (Early)</td>
<td>High</td>
<td>Must be followed by integrated study; only adequate when there is a low systemic tendency to build up intermediates</td>
</tr>
<tr>
<td>Correlation-Based Scale-Up</td>
<td>Low</td>
<td>Limited (Early)</td>
<td>High</td>
<td>Availability of correlations, property data and stable process regimes</td>
</tr>
<tr>
<td>Fundamental Approach</td>
<td>High</td>
<td>Full Applicability</td>
<td>High</td>
<td>Detailed theoretical understanding of system</td>
</tr>
<tr>
<td>Empirical Approach</td>
<td>High</td>
<td>Full Applicability</td>
<td>Low</td>
<td>None</td>
</tr>
</tbody>
</table>
Modeling is an essential part of scale-up when using any approach

- Modeling in scale-up can serve one of various purposes:
  - Prediction of process characteristics in unit operations: a model of the dynamics of unit operations is a necessary condition for ensuring the proper sizing and output of larger-scale units
  - Design and analysis of pilot, demonstration and commercial facilities: Integrative models that include all planned unit operations play an important role in assessing project characteristics at various scales, in addition to playing a critical role in modular scale-up studies prior to validation with integrated facilities
  - Prediction of commercial performance from pilot or pre-commercial/demonstration plant data: an essential goal of many scale-up studies is the accurate prediction of commercial performance of a process, which when linked to commercial facility design will determine economic viability and, often, the continued funding of a scale-up project
Various differing types of models exist, each suited to different situations in scale-up

- **Fundamental models**
  - Any model based on a theoretical understanding of the process mechanisms
  - Used to describe the system from first principles of thermodynamics, phase equilibrium, and kinetics
  - Residence time distribution models are used to treat continuous, steady state processes by understanding flow through closed and open systems
  - Nondimensionalization models attempt to use fundamental equations in their nondimensional forms to calculate the conditions necessary to achieve desired outcomes at large scale

- **Empirical models**
  - Seeks to describe macroscopic phenomena with a mathematical relationship that approximates physical behavior
  - Coefficients are fitted to these relationships from observed data
  - Process simulators
  - Process simulators, such as AspenPlus, Aspen HYSYS, ChemCAD, SuperPro Designer, and others have the capability to produce robust models of processes at various scales
It is important to understand the limitations of modeling in the context of scale-up studies

- Limitations imposed by data
- Limitations from bounded model complexity
- Limitations from boundary conditions
- Model validation:
  - Validation of model logic: Is the model constructed according to well-established principles and in a manner consistent with the system it is trying to represent?
  - Validation of model assumptions: Can each assumption in the model be justified in terms of correspondence with the physical system and desired precision or accuracy? Does the set of assumptions used omit essential boundaries or important process characteristics?
  - Validation of model behavior: Does the model conform to the analyst’s expectations in response to stimulus? Does the model adequately represent the process being modeled?
Early strategic considerations in planning start-up program

<table>
<thead>
<tr>
<th>Desired Scale</th>
<th>- Are significant quantities needed to break into market? - Does a market for the product exist?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Piloting and Demonstration Risks</td>
<td>- What is the commercial timeline? Is there enough time for piloting and demonstration? - During piloting and demonstration, are development samples needed to provide to customers?</td>
</tr>
<tr>
<td>Start-up Risks</td>
<td>- Does the commercial success of the project depend on a flawless initial production campaign? - Is there an alternative supply of material or intermediates available in case start-up problems limit the production rate? Alternatively, are there production intermediates valuable enough to be sold separately? - What is the impact of delayed start-up on launch strategy?</td>
</tr>
</tbody>
</table>
Fermentation Scale-up Issues

Performance prediction in fermentation scale-up

- Physical effects of scale
  - Fermenter geometry
    - Head space
      » Higher dissolved CO2
      » Foaming
    - Mixing
  - Strain characterization and effect on fermentative growth
    - Higher number of strain generations at scale
    - Decreases in yield and titer due to contaminants and other non-idealities encountered during normal operation
Specific scale-up issues in fermentation

- Contaminants, sterilization, and septic control
  - Contaminants virtually unavoidable with scale-up
  - Control of contamination depends either on eradicating all contaminants entirely or accepting some manageable level of contamination.
    - Contaminants may pose a competitive threat, consuming feedstock without producing the desired product, consume the microorganism or may poison the culture or produce an undesired by-product.
    - When a genetically modified yeast contaminated with a wild yeast. In these cases, there are few options besides full sterilization of the medium or further development of the organism to make it compete more effectively.

- Fusel oils
- Non-producing organisms
- Preferential feedstock utilization
Specific scale-up issues related to biomass supply

- Biomass supply and facility capacity
  - Dedicated land and captive biomass production as part of project scope
  - Local biomass productivity and variability
- Feedstock storage
  - Seasonality of biomass availability
  - Large scale receiving
  - Long-term storage without biomass degradation
  - Easy extraction for feeding the fermenter
  - Preprocessing to pellets
Conclusions

- A scale-up program for a chemical process is a compromise between capital cost minimization and process risk minimization within the constraints of time and cost of process development.

- Process innovation may take you into areas where your firm has little expertise or experience which has implications on scale-up costs.

- Scale-up is an art that requires the use of special models and judgments on the number of stages required from lab to commercial scale.
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- Numerous chemical business strategy engagements for biotech and other new technology companies

- Extensive financial consulting practice offering services for:
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  - IPO strategy
  - Due diligence
  - Joint venture development
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