Effective Bench to Pilot Transition
Benefits & Lessons Learned

Next Generation Bio-Based Chemicals
January 28, 2013

Allen Julian, Chief Business Officer, MBI
Discussion Topics

- MBI background information
- Bioprocess development – Bench to pilot transition
- Case studies
- Benefits & lessons learned
MBI: An Integral Part of the MSU BioEconomy Network

MSU Admin Offices
- MSU Technologies (Intellectual Property)
- MSU Business Connect (Corporate Engagement)
- MSU Contracts and Grants

Derisking and Scale-Up
- MBI for Bio-based Technologies, Bioeconomy Institute (Holland) for Chemical Process Technologies

Life Sciences
- Plant biology, Microbiology, Biochemistry, Molecular Biology, Chemistry, Ecology

Agricultural Sciences
- Michigan AgBioResearch
  Agronomy, Forestry, Crop and Soil Science, Animal Science

Policy
- Land Policy Institute, Environmental Science and Policy Program, Institute for International Agriculture, James Madison College

Outreach
- MSU Extension Services, Knight School for Environmental Journalism, Social Network Research

Sustainability
- Kellogg Long Term Biological Experimental Station, LCAs, Supply Chain, Center for Systems Integration and Sustainability

Engineering
- Chemical, Biosystems and Agricultural Engineering, Mechanical Engineering and related disciplines
MBI: Mission, Model and Capabilities

- Mission: Accelerate development, scale-up and commercialization of bio-based technologies

- Not-for-profit, founded in 1981, subsidiary of MSU Foundation

- Business model:
  1. License revenues from deployment of bio-based technologies for maximum societal benefit
  2. Corporate collaborations
  3. Competitive grants

- Capabilities: biomass pretreatment, microbiology/metabolic engineering, chemistry, bench (shake flask to 10-L) and pilot (up to 3,800-L) bioprocess development and scale up.
# MBI’s Technology Readiness “Sweet Spot”

<table>
<thead>
<tr>
<th>Phase</th>
<th>TRL</th>
<th>Maturity Level</th>
</tr>
</thead>
<tbody>
<tr>
<td>Commercial Deployment</td>
<td>9</td>
<td>Large-scale commercial operations</td>
</tr>
<tr>
<td></td>
<td>8</td>
<td>Semi-works-scale technology demonstration</td>
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<tr>
<td>Commercial Transition</td>
<td>7</td>
<td>Detailed engineering /plant design</td>
</tr>
<tr>
<td>Viability Demonstration</td>
<td>6</td>
<td>Scale up and pilot-scale technology validation</td>
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<tr>
<td>Technology Development</td>
<td>5</td>
<td>Production enhancements/techno-economic model</td>
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<tr>
<td>Feasibility Demonstration</td>
<td>4</td>
<td>Lab-scale development and integration</td>
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<tr>
<td>Basic Research</td>
<td>3</td>
<td>Lab-scale experimental proof of concept</td>
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<tr>
<td></td>
<td>2</td>
<td>Technology application formulated</td>
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<tr>
<td></td>
<td>1</td>
<td>Promising research finding</td>
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## Transition from Bench to Commercial Scale

<table>
<thead>
<tr>
<th>Phase</th>
<th>Scale (L)</th>
<th>Maturity Level</th>
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<tr>
<td>Commercial Deployment</td>
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<td>Large-scale commercial operations</td>
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<td>Commercial Transition</td>
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<td>Semi-works-scale technology demonstration</td>
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<tr>
<td>Viability Demonstration</td>
<td>1000</td>
<td>Scale up and pilot-scale technology validation</td>
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<tr>
<td>Technology Development</td>
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<td>Production enhancements/techno-economic model</td>
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<tr>
<td>Feasibility Demonstration</td>
<td>0.01</td>
<td>Lab-scale development and integration</td>
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<td>Basic Research</td>
<td>0.001</td>
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Projects can enter the pipeline at any stage
Pipeline typically includes a mix of internal projects and external collaborations
MBI’s goal is to deploy viable technologies broadly for maximum societal benefit
Discussion Topics

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• Bioprocess development – Bench to pilot transition
• Case studies
• Benefits & lessons learned
Bioprocess Development: Strain Engineering

- Classical Approaches
  - Mutagenesis
  - Screening and selection
  - Adaptation

- Metabolic Engineering Approaches
  - Flux improvements
  - Byproduct minimization
  - Pathway design: novel enzymes and routes

- Strain Stability Considerations
Bench-scale Bioprocess Development: Scalable by Design

- Metabolic Insights
  - Growth/Biosynthesis interface
  - Pathway bottlenecks
  - Process control schemes

- Fermentation Process Performance
  - Fed-batch/continuous modes
  - Dissolved Gases
  - Design of experiments

- Bioprocess Integration
  - Raw material qualification
  - Product recovery and purification
  - Recycle streams
MBI Bench Scale Capabilities

- 20 fermenters (2 to 5 L)
- Automated control /acquisition
- Full analytical support
Bench to Pilot Transition
- Mass Transfer Considerations
- Process Control
- Downstream Process Integration
- Techno-economics
**Mass Transfer Considerations**

- Supporting aerobic metabolism

<table>
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<tr>
<th>Scale</th>
<th>Oxygen Transfer (mmoles/L.h)</th>
<th>Mixing Time (s)</th>
</tr>
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<tbody>
<tr>
<td>Bench</td>
<td>~400</td>
<td>~1</td>
</tr>
<tr>
<td>Pilot</td>
<td>~200</td>
<td>~30</td>
</tr>
<tr>
<td>Commercial</td>
<td>~100</td>
<td>~100</td>
</tr>
</tbody>
</table>

- Hydrostatic pressure and carbon dioxide sensitivity
Pilot-Scale Observations & Outputs

- Broth properties impact recovery
- Product quality
  - Impurity profiles
  - Batch to batch variance
  - 10’s to 1000’s of pounds of test material
- Accurate mass and energy balances
- Downstream processing equipment performance
- Design and evaluation of recycle streams
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MBI Case Study: Bio-based Fumaric Acid

- **Performance Improvements:**
  - 3-fold increase in volumetric productivity to 1.8 g/l.h
  - 10% increase in titer to 80 g/l
  - Maintained yield of 0.6 g/g of sugar
  - Simplified 2-step recovery integrated with fermentation

- **Starting point was a highly developed technology**
  - Filamentous fungus (*Rhizopus*)
  - Aerobic process
  - Novel approach was developed to control morphology

- **Integrated process scaled successfully to 3,800-L**
Performance Improvements:
- >2-fold increase in volumetric productivity to >2.5 g/l.h
- 70% increase in titer from 70 to >120 g/l
- 40% increase in yield from 63% to >90% of theoretical yield on sugar

Other improvements
- Eliminated yeast extract as a required nutrient
- Reduced cost using novel base recycle scheme
- Anaerobic organism *Actinobacillus succinogenes* isolated from rumen by MBI

Integrated process scaled successfully to 3,800-L
AFEX™ Pellets: A Versatile Biomass Commodity

- Biorefinery sugar feedstock
- Releases 75+% of sugars for fuels and chemicals
- Ruminant animal feed for beef and dairy cattle
- Potential to displace corn grain
AFEX™ Biomass Pretreatment

- Applicable to variety of ag residues
- Dry-in, dry-out, no waste process
- AFEX pellets 9-fold denser than biomass
- Stable, storable, readily transportable

Raw Biomass  
Treated Biomass  
AFEX Pellets
AFEX: Proven Effective on Variety of Ag residues

Experimental results from Bruce Dale lab, MSU
AFEX System: Gen-3

- Demonstrated $\text{NH}_3$ absorption, desorption, and transfer from bed to bed
- Performance in 10 L prototype met batch reactor benchmarks with
  - Corn stover
  - Wheat straw
  - Oat hulls
  - Switchgrass

Unique features:

- Simple operation
- Simple ammonia recovery
- Low capital cost
- Can be scaled to the right size for local biomass center close to farm

MBI-led team (MSU, INL) wins $5.3$ mil DOE/EERE grant for 100-fold scale up in 2011
Reactor Size: 1000 liters
Throughput: 1 ton/day
Installation: Early 2013
MBI Case Study: AFEX Biomass Pretreatment

- Performance:
  - Simple low-cost packed bed reactor design
  - Ammonia recovery demonstrated at >95%
  - 75+% sugars at high >20% solids loading
  - AFEX treated biomass can be densified up to 9-fold
  - Sugar cost matches corn sugar benchmarks

- Currently in process of installing 1TPD pilot reactor
  - Cattle feed trials planned for Spring 2013 with 40 tons
  - Pilot scale biomass hydrolysis/fermentation Fall 2013
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Benefits of Bench to Pilot Transition

- Generates techno-economic analyses with solid empirical data
- Provides robust performance and engineering data for transition to semi-works or commercial scales
- Makes 100 – 1000+ kg representative product for end-use applications testing and qualification
- Reduces risk and increases confidence to move toward commercial scale
- Attracts capital investment and partners to accelerate commercialization
Accelerate Value Creation With MBI

- Opportunity: Create value by collaborating with MBI to accelerate commercialization of bio-based technologies

- Advantages:
  - MBI focused exclusively on de-risking bio-based technologies
  - Systematic, disciplined, efficient derisking process
  - MBI’s non-profit status enables close collaboration
  - Access to MSU BioEconomy Network
  - Fully integrated facility – biomass pretreatment, microbiology, chemistry, fermentation, down-stream processing
  - Proven track-record of successful collaborations
Thank-you for your time and interest

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