Fast track Technology Transfer from R&D to Commercial Production of Renewable Food & Flavor Ingredients:
Global Platform & Reb M

Edi D. Eliezer
Sr. V.P. Engineering & Manufacturing

Outline
- Why Renewable F&F* by Biotechnologies?
- Bioprocess Technology & Scale-up
- Conagen’s R&D and Manufacturing capabilities
- Conagen’s F&F examples & Success stories

(*) F&F: Food & Flavor ingredients

Limitations of Natural F&F* Product Extractions
- Long growing season
- Unsustainable natural resources
- Low concentration of actives
- Climate changes and natural disasters affect availability, quality and price
- Contamination of natural sources is a common problem

Natural variation affects production Costs & Quality

(*) F&F: Food & Flavor ingredients

Why Renewable F&F Products by Biotechnology?
- Sustainability
  - Availability of feedstock for bioprocesses is relatively more stable than special natural ingredients
- Quality: more consistent than nature
  - Better control of bioprocesses lead to Quality Products
- Cost
  - Global costs of major feedstock for bioprocesses are relatively more stable than special natural feedstock

Typical BioProcess Block Flow Diagram (BFD)

Utilities:
- Process Water
- Steam
- Cooling Water
- Chilled Water
- Compressed Air
- Electrical
- HVAC
- Waste Systems

Bio / Microbial Labs.

Fermentation or Bioconversion

Recovery & Purification

Finishing

Media Prep / Sterilization

Solutions Prep/ Storage

Warehouse: Raw Materials

Product

Key Factors for Bioprocess Technology Selection, Scale-up & Engineering of New Facilities
- Biocatalyst
- Raw Materials
- Technologies
- Products
- Scale
- Economics

For "FAST-TRACK"
- Focus Very Early on 'Few Key Parameters'
- Implement Very Early 'Integration' across Technical & Business lines
Conagen Mission & Facilities

- Vertically Integrated company from Discovery to Commercialization, Globally Competitive
- R&D facility in Boston area for early to late Strain & Process Development from minibioreactors to Pilot scale fermenters
- Manufacturing facilities in China to satisfy Conagen’s and Clients production needs in a very competitive way

Conagen is a Developer & Supplier of Renewable Natural Ingredients through Biotechnologies

- Focus on Development and Production of high value natural ingredients for Food & Flavors industries
- Scientists in synthetic biology develop new strains, metabolic pathways, enzyme & cell control mechanisms (using HTS at many stages) for optimal biocatalysts
- Bioengineers in advanced fermentation & bioconversion technologies perform Process Development & Scale-up to Pilot scale proof of concept and Commercial Manufacturing
- Typical products developed: terpenoids, sweeteners, flavors

Industrial Manufacturing

Current Fermentation Plant (AH)

AH Fermentation Building

New BioManufacturing Complex
New BioManufacturing Complex - Design Basis

- Commercial Manufacturing with segregated Fermentation, Extraction (XP/ATX), Media Preparation and Utilities buildings
- Multiple large scale (>100m³) Fermentation trains for Multiproducts, with extra space for future expansion
- Multiple DSP trains designed as independent modules
- Separate independent semi-commercial Pilot Plant
- Quality in design and operations: GMP, Kosher and Hallal

Conagen’s Success stories

- 26 patent families developed internally – 100+ global filings
- Conagen has successfully moved 14 products from benchtop to large scale production

Conagen’s Natural Product by Biotechnology: Natural Sweeteners

- Sugar intake becoming a health issue (e.g. diabetes)
- Sugar replacement is a $90 billion global market
- Current low-calorie sweeteners are unsatisfactory (e.g. artificial, taste issues)
- 30% of sugar estimated to be replaced by non-caloric, non-artificial sweeteners by 2021
- Heavy investment in new generation natural sweeteners
The Solution to the problem

- Next generation, nature based Stevia product (Reb-M) that has a taste comparable to table sugar
- Water soluble for use in diverse food & beverage applications
- Non-GMO based ingredient that is demanded by food & beverage companies
- Economically viable sweetener ingredient
- The only commercially available Reb-M product produced today (to our knowledge)
- Sustainable production in a food grade GMP plant

As close to sugar as you can get

Sensory mapping shows just how close BESTEVIA™ Reb-M stevia sweetener is to Sucrose

Greater sweetness and less bitterness

Sensory mapping shows BESTEVIA™ Reb-M stevia sweetener has a higher concentration of sweet taste and significantly less bitterness and aftertaste than Reb A

Conclusions on Success factors for Fast track Scale-up to Global Commercial Manufacturing

- Integrate, early on, R&D, Engineering, Manufacturing and Business across local & global boundaries
- Very early on, Focus on few key parameters & process options with major impact on Scale-up & Manufacturing Costs
- Focus on Fast-track Kilo’s sample Manufacturing to prove new commercial product feasibility & purity profile
- Integrate & optimize global R&D and Mfg. resources & costs
- Keep constant communication to understand and appreciate technical & cultural differences across global sites

Ending on a sweet note

thank you!