DEVELOPMENT DELIVERY SUPPLY

Flexible Manufacturing Strategies

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Speakers

Dr. Alton Johnson is Principal at NGT Biopharma Consultants, and Owner of Alton Johnson Consulting, LLC. Alton Johnson is an industry leader in technology and innovation, manufacturing science and technology, and product and process development. Alton has 31 years of experience in manufacturing and research and development. He holds a Doctor of Philosophy Degree in Industrial and Physical Pharmacy from Purdue University and a Bachelor of Science Degree in Pharmacy from University of Carolina, Chapel Hill.

Katie Noah is a Pharmaceutical Research and Development Project Manager at Catalent's Winchester, Kentucky facility. Katie has been with Catalent for the past six years and has experience in supply chain and quality control. She is responsible for facilitating technical transfers to the site and assisting our customers through development to process validation. Katie has an undergraduate degree from Purdue University and a Master's Degree in Business Administration from The University of Kentucky.

Key Learning Objectives

- Factors that have led to the increased need for flexible manufacturing
- Strategies used to implement flexible manufacturing
- Benefits of flexible manufacturing strategies
- What to look for when selecting a partner who offers flexible manufacturing
- The use of different technologies that are easily scalable and reproducible

Drivers of Flexible Manufacturing

- Lower commercial product volumes
- Reduced peak sales period
- Accelerated development timelines
  - Unmet patient need with expedited regulatory pathways
  - Innovative clinical study designs
  - Quality by Design, risk management
  - Post-launch studies, lifecycle management
- Digitally enhanced data acquisition & analysis
  - Risk management
  - Knowledge management
  - Data integrity
  - Compliance

Accelerated Development Timelines

What percentage of NDAs are designated as expedited as of mid-year 2019?

Fast Track, Accelerated Approval, Priority Review, Breakthrough Therapy

a. 12%
b. 27%
c. 38%
d. 65%
e. 85%

Reference: FiercePharma, Aug. 2019

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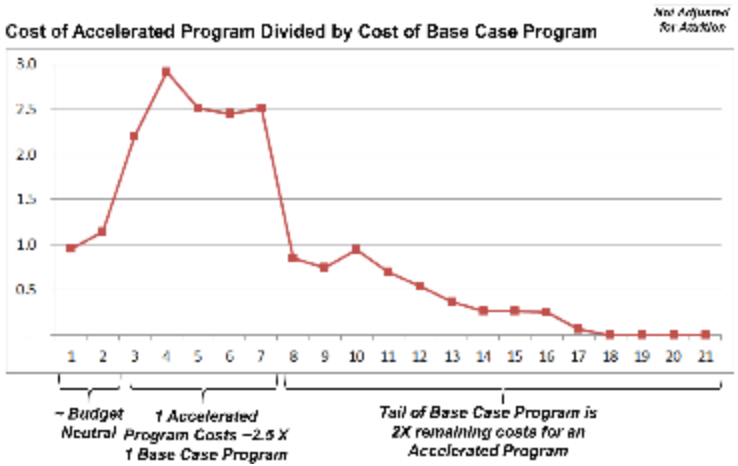
Approaches for Flexible Manufacturing

Conventional

- Increased risk: scale-up and technology transfer
- Resource intensive
- Limited to few development programs



Reference: Spavins Consulting, LLC

Approaches for Flexible Manufacturing

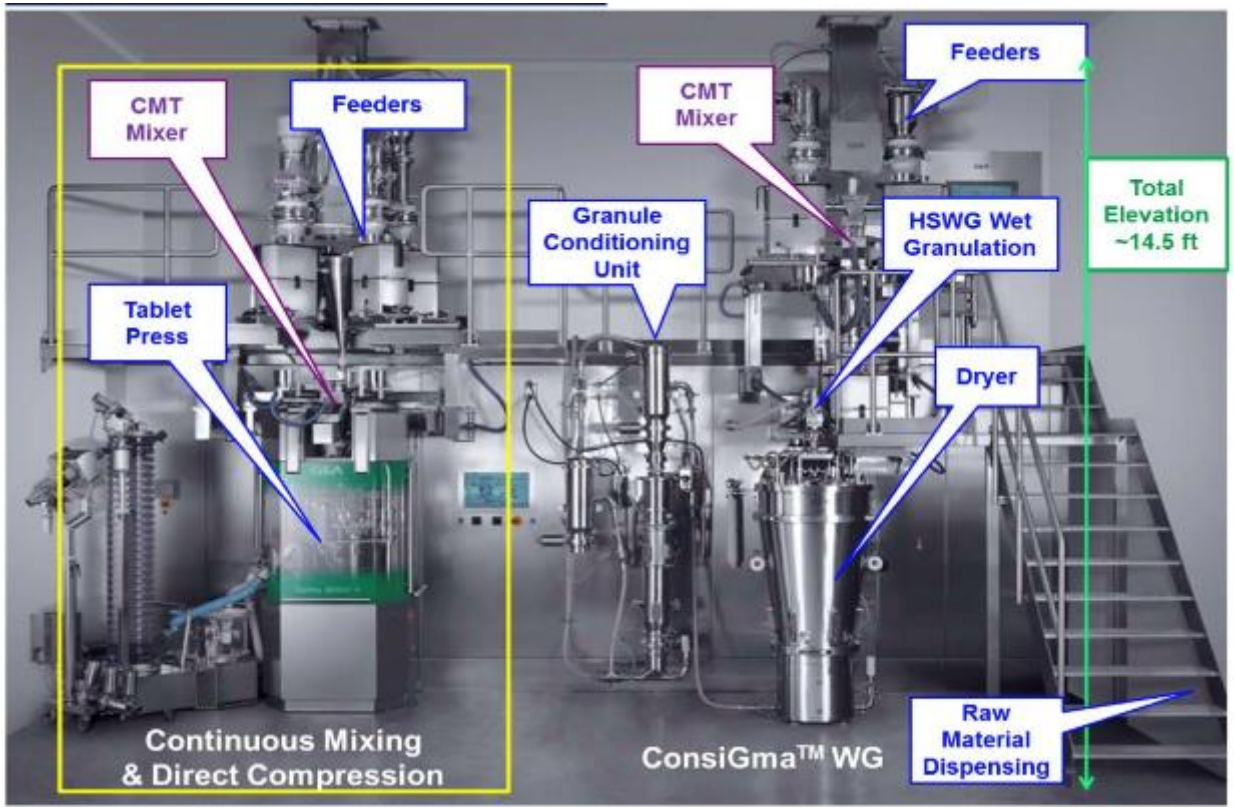
- Modular (skids or inserts into standard facility)
  - Fixed, flexible factory space
  - Faster time to equipment commissioning
  - Direct technology transfer (like-for-like equipment)

- Podular (skids or inserts into pod-built factory)
  - Movable, faster to build, smaller footprint & lower cost facilities
  - Faster time to equipment commissioning
  - Direct technology transfer (like-for-like equipment)

Manufacturing PODS

Reference: www.gconbio.com

Portable Continuous Miniature Modular



Reference: www.ispe.com

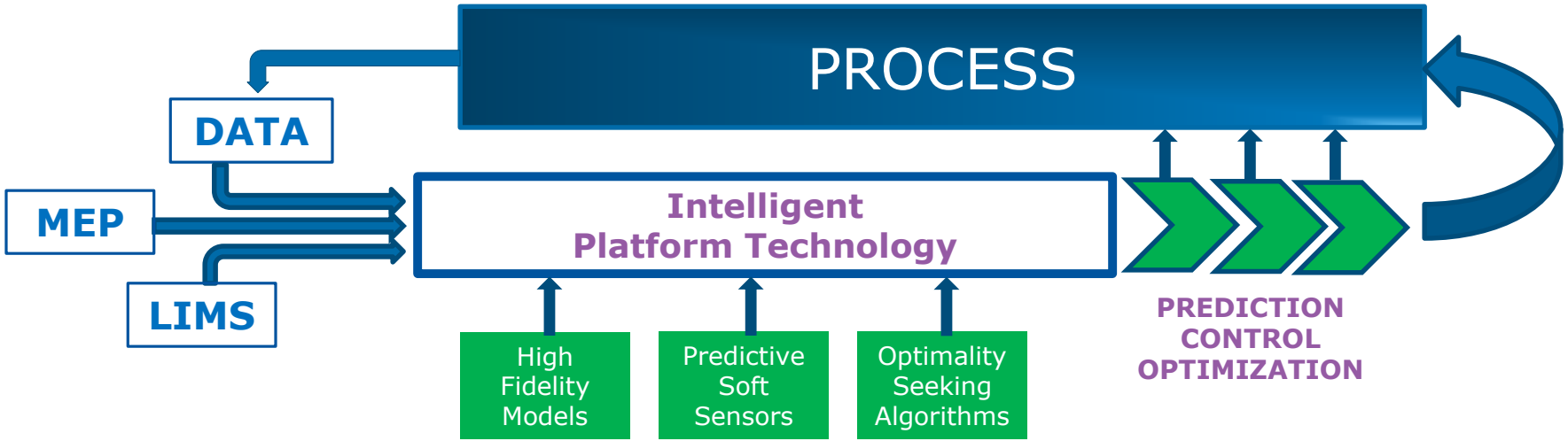
Some Recent New Commercial Products Manufactured by Continuous Processing

Year	Product	Therapeutic Category	Company
2015	Orkambi™	Orphan – cystic fibrosis	Vertex
2016	Prezista™	Infectious Diseases - HIV	Janssen
2017	Verzenio™	Oncology – metastatic breast cancer	Eli Lilly
2018	Symdeko™	Orphan – cystic fibrosis	Vertex
2018	Daurismo™	Oncology – leukemia (AML)	Pfizer

IoT / Digitally Enabled Data Analysis

- Harness the complementary power of data, models, engineering and IT infrastructure to create a game changing paradigm based on:
  - Transformation of data into knowledge and intelligence
  - Moving from reactive actions into proactive and preventative strategies
  - Shifting from stand-alone and isolated unit operations towards integrated infrastructure at process, plant, and enterprise levels

Digital Enabled Advanced Process Control and Process Optimization



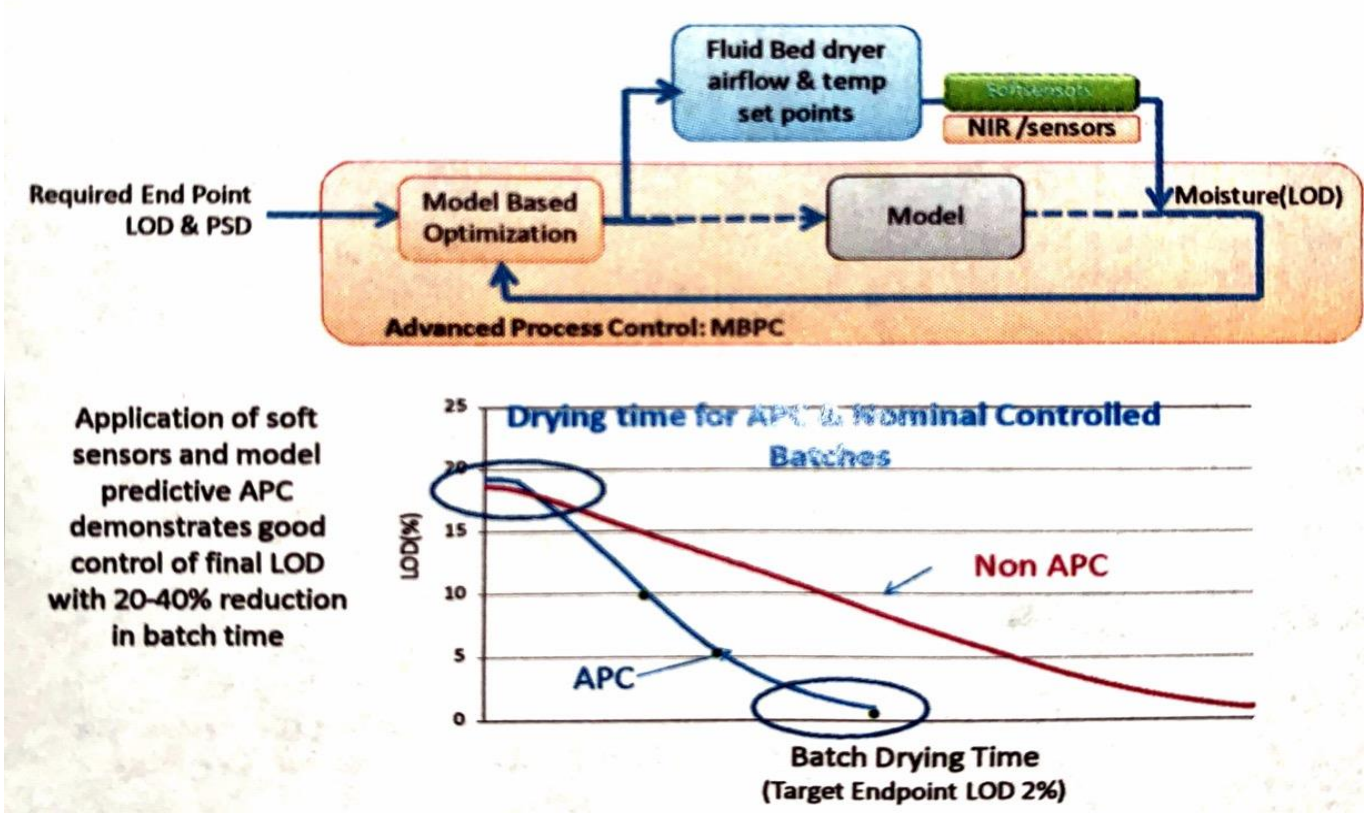
DEVELOPMENT

Reverse Engineering (PSD, CU, Dissolution)
Rapid Development (50% less DOE)
Robust Scale-up (Scale Insensitive)

MANUFACTURING

Reduced Variability (50-60%)
Increased Productivity (25 – 40%)
Reduced Energy (10 – 15%)

Particle Size Prediction Model



Flexible API Supply Technologies

A series of small footprint, portable, flexible and continuous development and manufacturing technologies that can be integrated into batch infrastructure to simplify unit operations

Pfizer has a focus on two primary benefits of continuous processes:

1. Ability to design a platform to meet chemical process requirements → Optimize mass transfer, heat transfer, residence time, etc. **QUALITY, SPEED**

2. Ability of continuous processing to greatly simplify unit operations → Design highly efficient processes **AGILITY, COST**

Reference: Nicholas Thomson, Senior Director, R&D, Pfizer, Inc.

Benefits of FAST

The same equipment can be used at different stages of development bringing significant ability

Cycle Time

Demand

Transfer

Modular

Quality

Sustainability

Reference: Nicholas Thomson, Senior Director, R&D, Pfizer, Inc.

Key Benefits for Flexible Manufacturing

- Lower capital and operations costs
- Faster deployment (50% reduction)
- Reduced risk
  - No scale-up
  - 'Like-for-like' tech transfer
  - Integrated digital solutions, real-time
    - Integrated automation, PAT, APC, data analysis
- Potential for faster changeover
- Supply flexibility

Catalent

Flexible Manufacturing

KATIE NOAH, PROJECT MANAGER, CATALENT

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Flexible Manufacturing is the ability to fulfill our customers needs through employing known techniques and processes to achieve the project's requirements. It can entail scale-ups, equipment transfers/purchases, or designing a manufacturing process to meet the project's specific requirements.

- Flexible Manufacturing has several key benefits:
  - Conserving API and materials
  - Developing a process that is scalable (10x rule)
  - Ability to customize
  - Optimization of the current process

- Having a strategic partnership is key

Case Study 1: Partnership Advantages

Summary: Catalent worked with a customer on two of their projects, however, the customer was having quality issues with a program placed with a CMO and their product was pending submission and had already completed the registration process. The CMO was using a piece of equipment Catalent didn't have in its inventory at the time.

- Challenges
  - Timing
  - Leveraging Catalent's global network & expedited equipment sourcing
  - Feasibility campaign was run prior to a successful registration campaign
- Solutions
  - Catalent sourced the equipment from another site in our global network
  - Validation was expedited through leveraging the original site's validation work
  - The timeline was met

Case Study 2: Customized Manufacturing

Summary: A large multi-national company was looking for a manufacturer to produce a drug with the potential to save lives, and offered drastically improved administration with a new mechanism of delivery.

- Challenges
  - Trouble finding partner with right equipment and capacity to accommodate the project's specific needs
  - New mechanism of delivery
- Solutions
  - Catalent built a customer suite in its Winchester, KY facility to manufacture the combination device
  - Because Catalent had anticipated demand, five rooms were constructed within fallow space at the site
  - Much of the necessary equipment and appropriate infrastructure was already in place
  - Outcome: The FDA approved commercialized project in 2019

Case Study 3: Scalable Solutions

Summary: A customer had the opportunity to be 'first-to-file' of a controlled API. Registration to be performed on a GPCG-60 fluid bed after one feasibility batch.

- Challenges
  - Due to limited time, could not scale-up prior to registration
  - Batch size was not optimal for launch and commercial-scale supply
  - API constraints for process scale-up prior to validation
- Solutions
  - Placebo batch run to assess feasibility and ensure the batch would properly fluidize
  - Were able to proceed based on confirmation of successful physical testing
  - Successfully scaled-up to support launch volumes required

Expansive Global Network of 14 Oral Development and Manufacturing Facilities across North America and Europe

ACCELERATED DEVELOPMENT	**Capacity** and **flexibility** for faster timelines with dedicated expertise.
INTEGRATED SOLUTIONS	**Start Here. Stay Here.** Catalent's integrated network of science-driven development and commercial manufacturing sites facilitate faster development with reduced risk and seamless scale-up to commercialization.
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