



II Всероссийская GMP-конференция

18-20 сентября 2017 года
Геленджик



Current Status Continuous Manufacturing of Oral Solid Dosage Forms

Typical Industry Examples & Show Cases

Oskar Goldstein
Regional Support Manager
GEA APC Pharma Solids
18 September 2017



Pharmaceutical market; megatrends

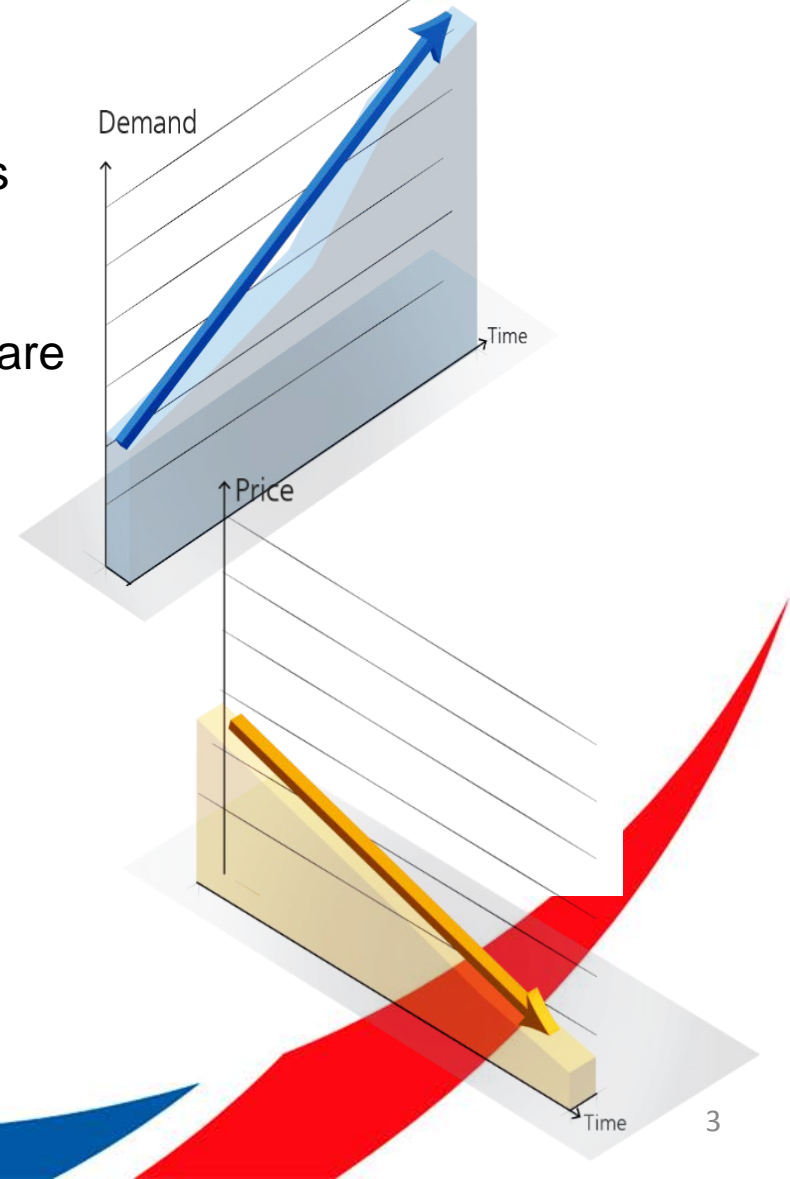


II ВСЕРОССИЙСКАЯ
ГМР КОНФЕРЕНЦИЯ

- Generic and prescription free drugs
- Ageing population
- Growing middle classes in emerging markets
- Increased patient safety
- Cost reductions in public and private healthcare
- Increased regulations
- Shift towards cheaper drugs
- Blockbuster patents are running out

Future production trends:

- Larger volumes for less cost
- Smaller volumes of specialized drugs



Why Innovation?



U.S. Food and Drug Administration
Protecting and Promoting Public Health

www.fda.gov

Pharmaceutical Manufacturing: The Path Ahead..

*“ Right now, manufacturing experts from the 1950s would easily recognize the pharmaceutical manufacturing processes of today. It is predicted that manufacturing will change in the next 25 years as current manufacturing practices are abandoned in favor of cleaner, flexible, more efficient **continuous manufacturing**. ”*

Dr. Janet Woodcock, AAPS Annual meeting, October 2011

“The lack of agility, flexibility, and robustness in the pharmaceutical manufacturing sector poses a potential public health threat as failures within manufacturing facilities that result in poor product quality can lead to drug shortages. Drug shortages are a critical health care issue, affecting individual patients across the United States. Recognizing that shortages commonly begin with a supply disruption related to product quality, FDA is focusing on encouraging and sustaining advancements in pharmaceutical manufacturing.”

When is OSD production successful?



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Success factor #1

Regulatory Agencies
Efficacy & Patient Safety



Success factor #2

Patient
Efficacy, Patient Safety & Affordability



Success factor #3

Pharma Industry
Efficacy, Patient Safety, Affordability
& Profitability

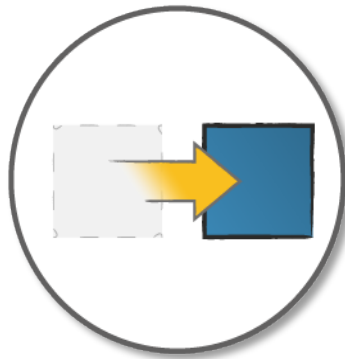




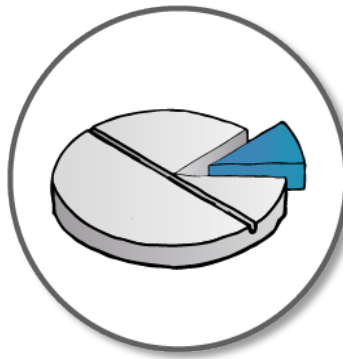
What to innovate?



No
Scale-up



Easy product
transfer



Variable
Production rates



Reduce
Time to Market



Cost reduction





Drivers for continuous manufacturing

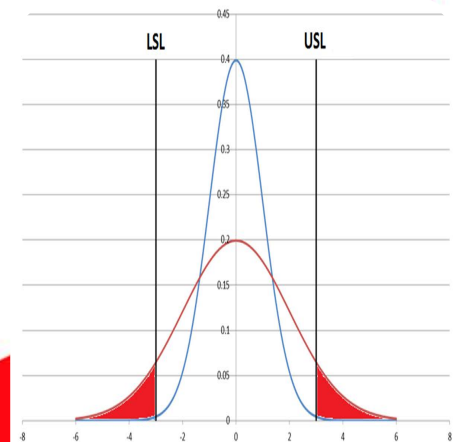
1. To improve the quality of pharmaceutical end products – **six sigma process**

- by focusing on **quality during the whole lifecycle** of the product and not just “tested in” quality
- understanding the **capability** of your processes and **manage the risks** caused by sources of variability

2. To manufacture in a cost efficient way – **lean manufacturing**

- by collecting **more information in R&D phase** in short time with less product
- by excluding risky, time and product consuming scale-up exercises
- by introducing **online measurement** and closed loop control targeting **real time release**, reducing waste to zero
- by incorporating flexible batch size (JIT production), **reducing inventory**
- by reducing energy cost per tablet, **reducing environmental impact**

Introduction to Continuous Manufacturing

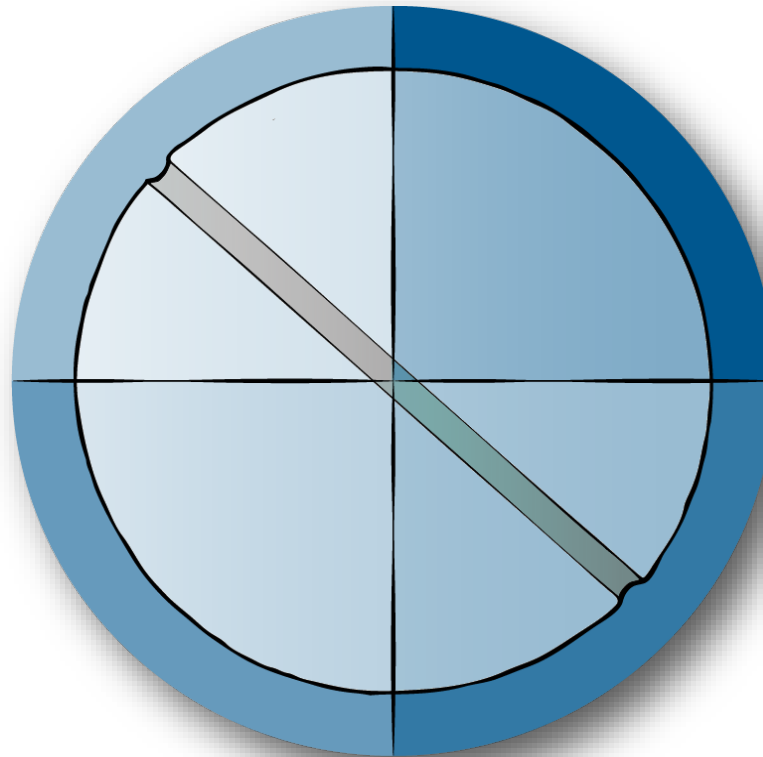




Agenda

Case studies

How does it work?



Competitive arena

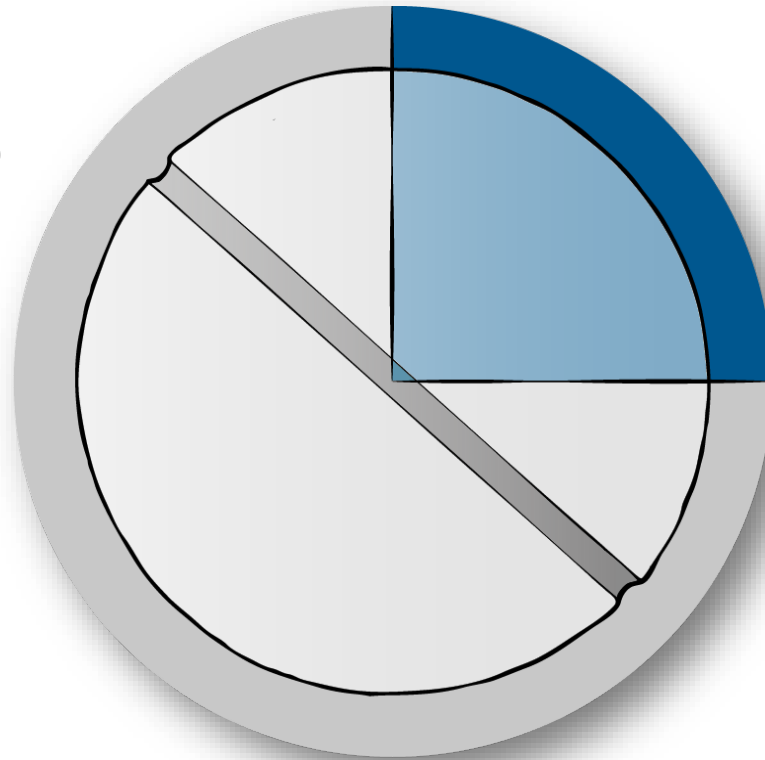
CM Landscape



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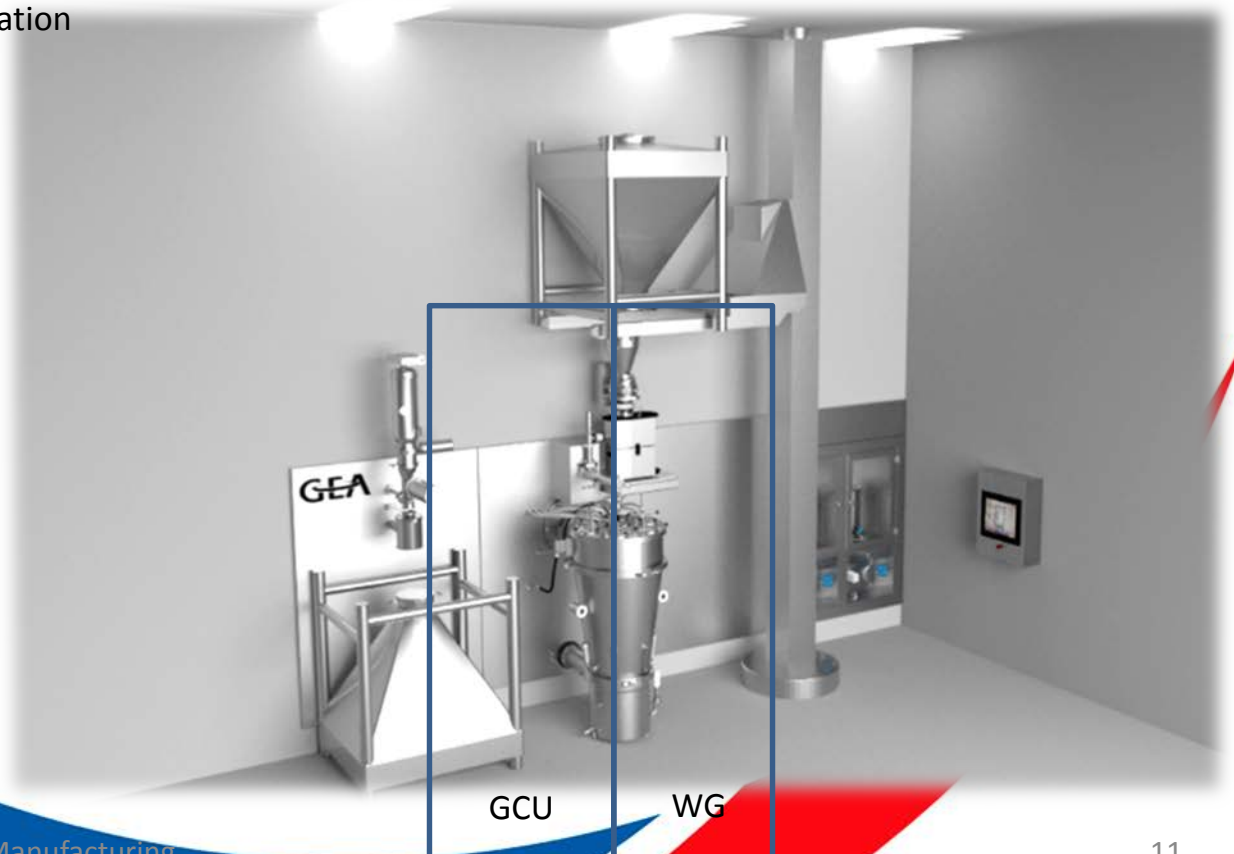
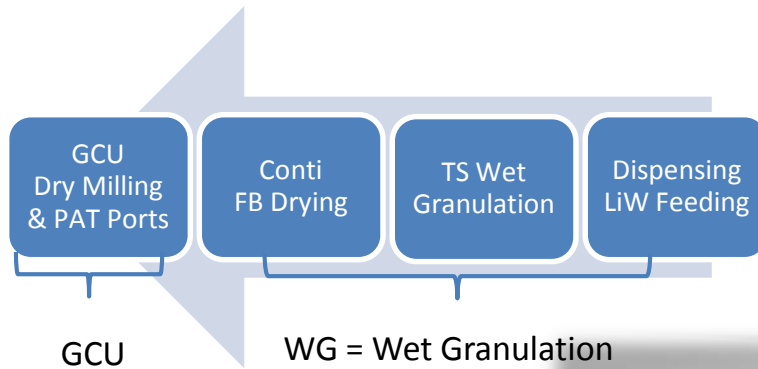


Competitive arena

CM Landscape



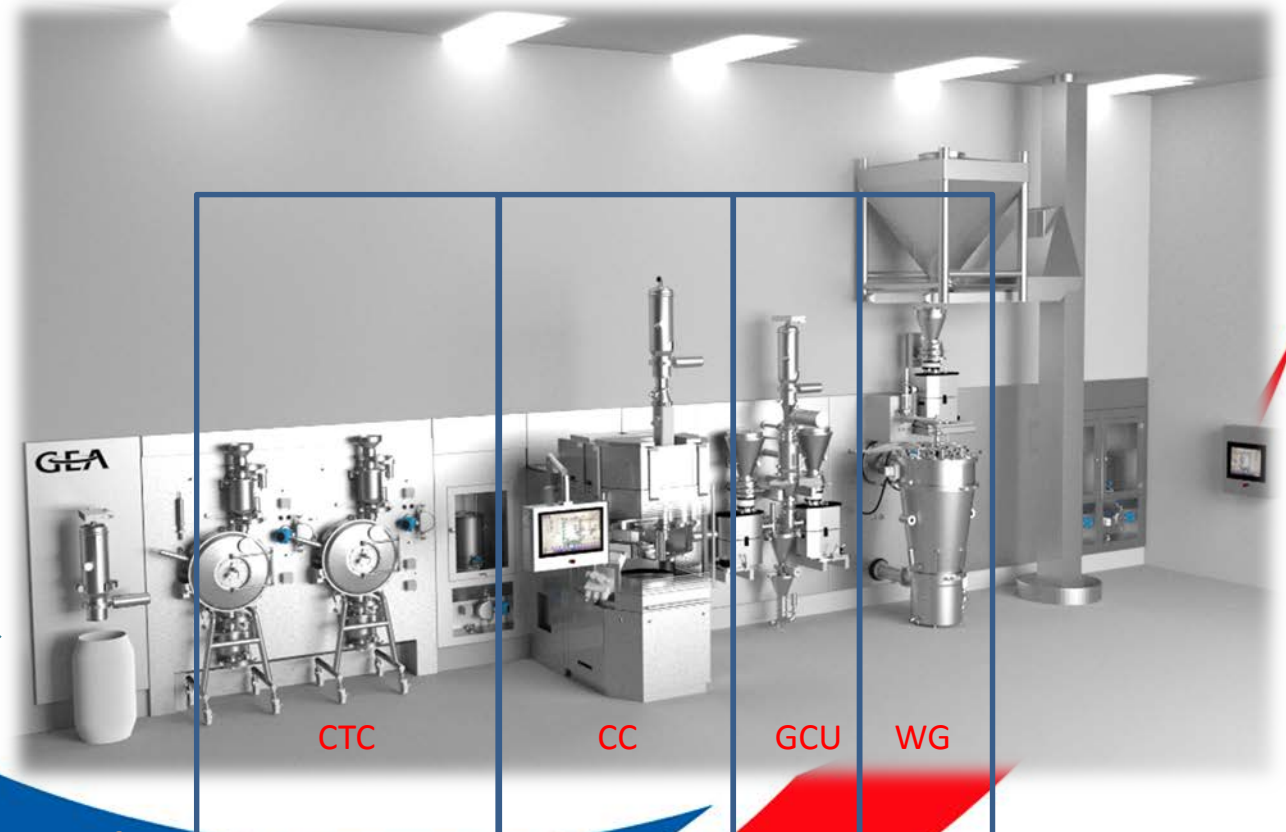
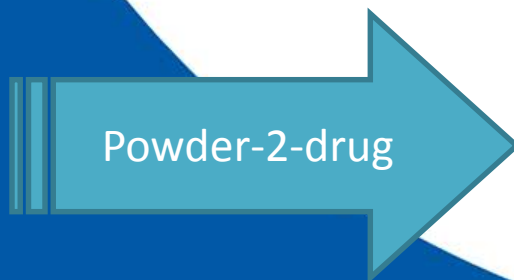
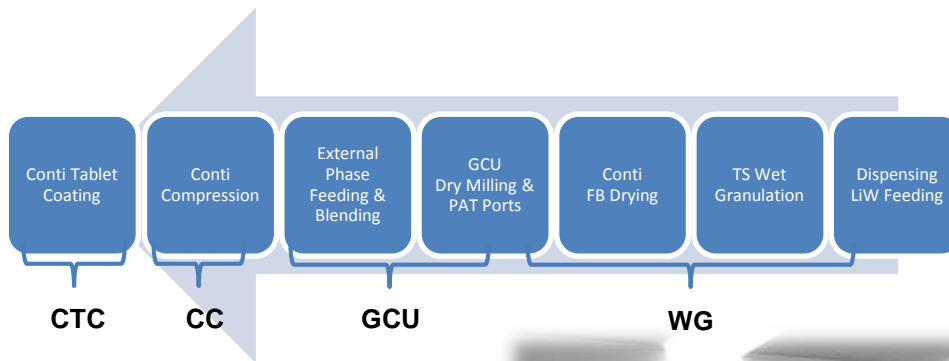
ConsiGma 25™ – Wet Granulation



Bin-2-Bin

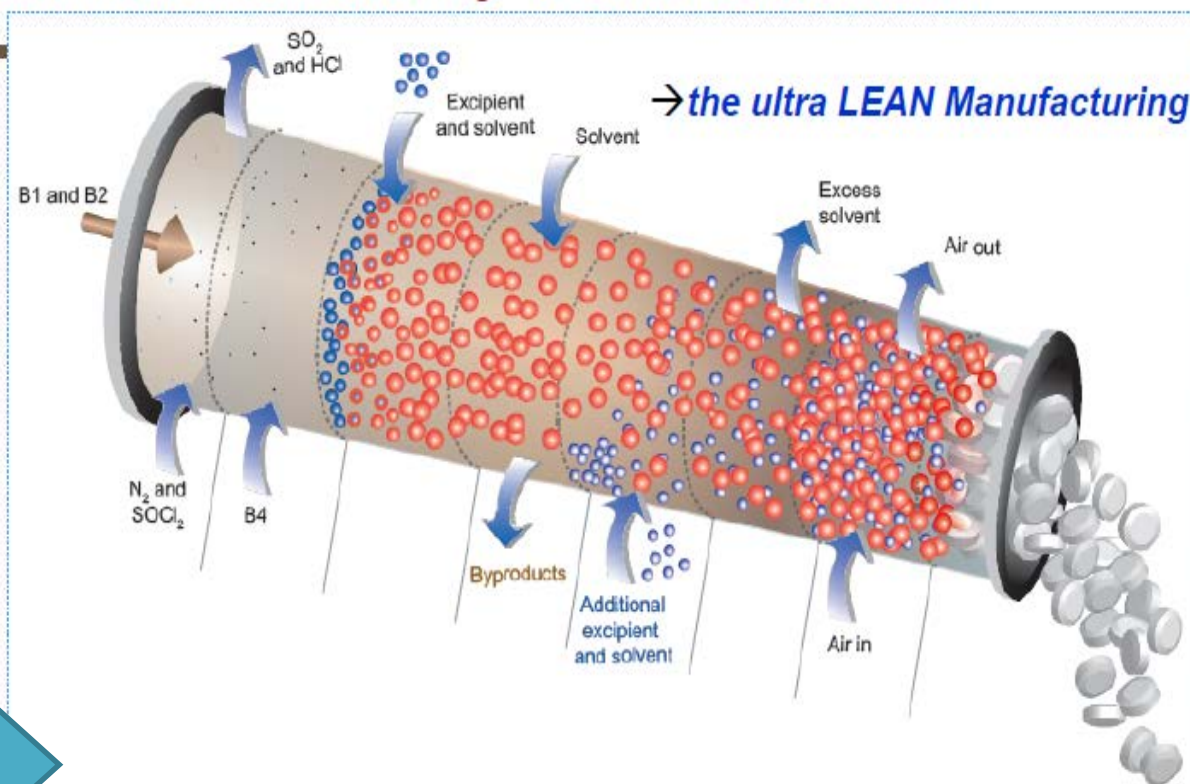


ConsiGma 25™ – CTL



Blue Sky Vision @ Novartis

Novartis-MIT Blue Sky Vision Continuous Manufacturing: *A radical transformation*



Active substance-
2-drug

From start of chemical synthesis through final pharmaceutical dosage form



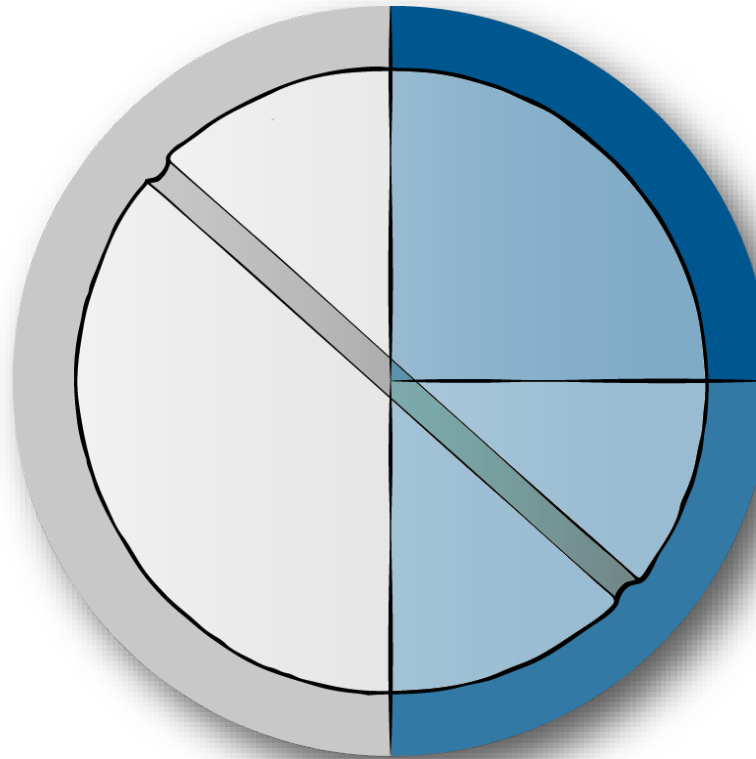
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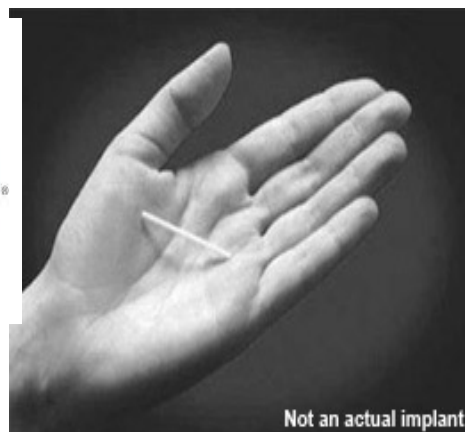
Competitive arena

CM Landscape



Bin-2-bin and powder-2-drug cases


Belsomra
(suvorexant) (IV)
5, 10, 15, 20 mg tablets



NUVARING



KALETRA



REZULIN



Grünenthal TRF technology

Intac – Powder-2-Drug Product

Extended Release

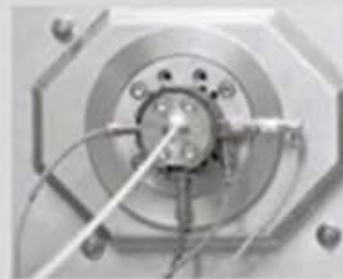
Core Technology

Immediate Release

Cooling & Cutting



Hot-Melt-Extrusion



Micro Pelletization



TRF ER Extrudates



Properties	Extrudates	Pellets
Surface	small	large
Dissolution	slow	fast
Crush resistance	✓	✓
Gelling	✓	✓

TRF IR Pellets



Current CM „Powder-2-drug“ products on the market



Chinoin



Vertex

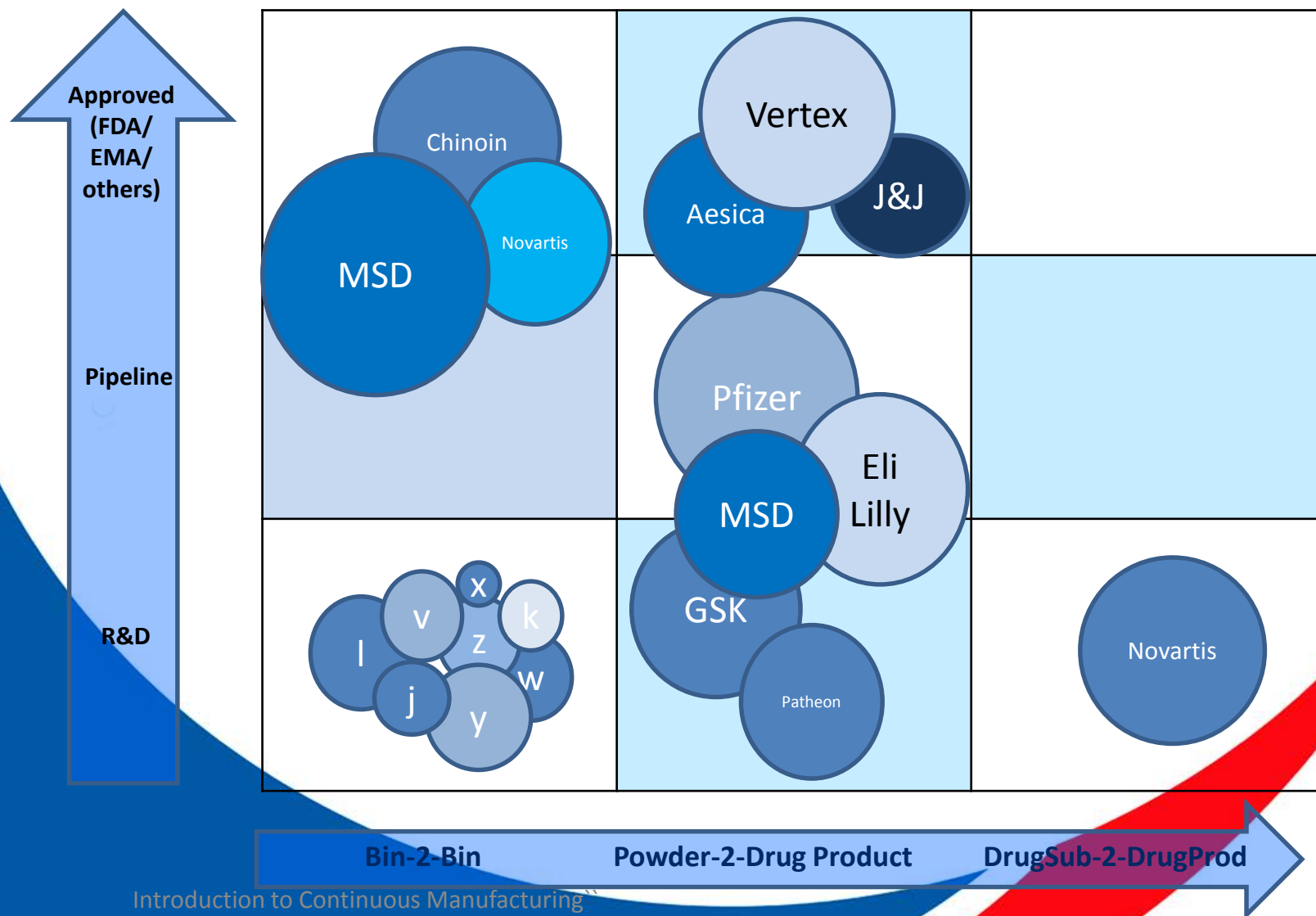


Janssen



**At Least 3 Products on the Market;
who is next?**

CM landscape grid by products & technologies 2016





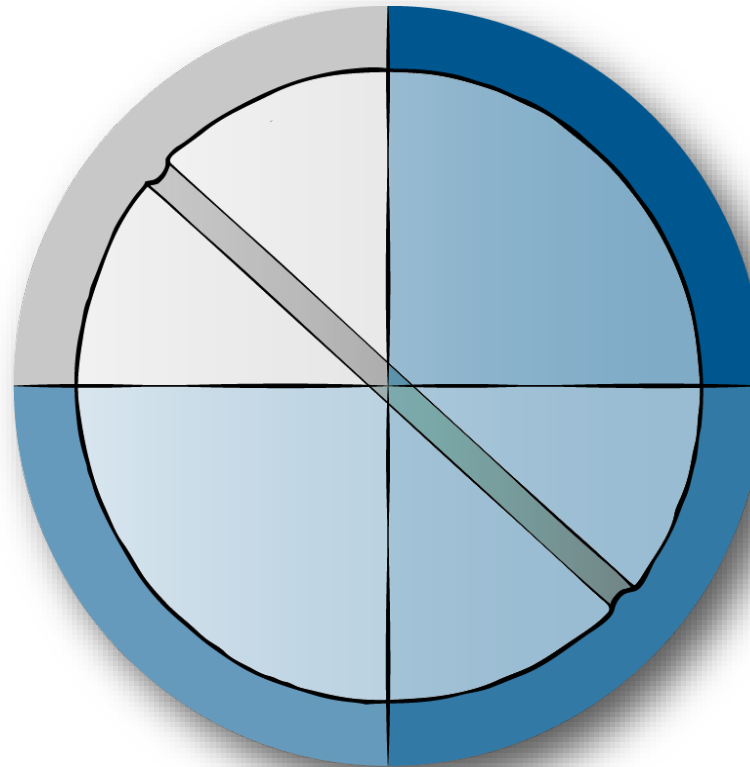
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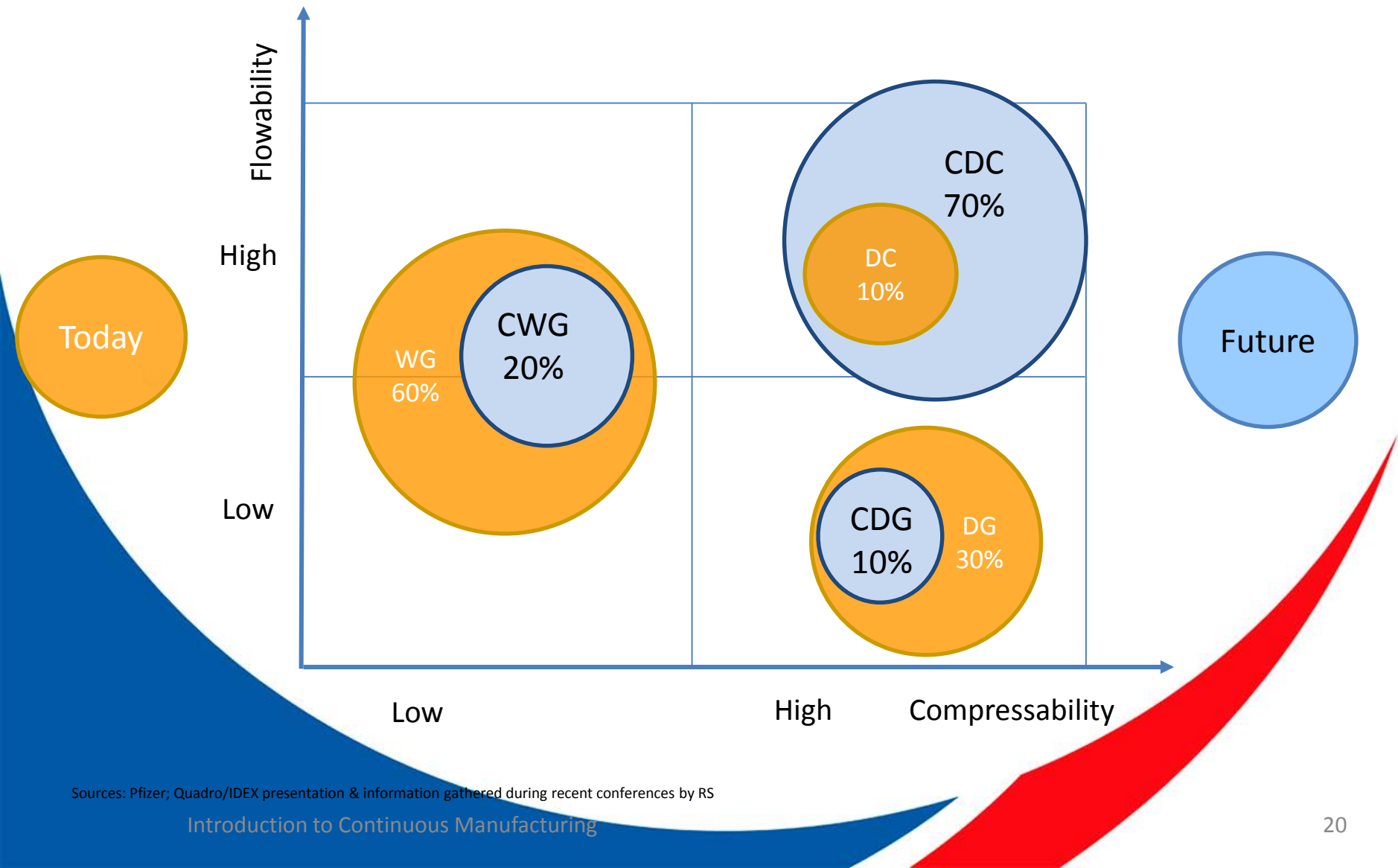
Competitive arena

CM Landscape





Threat of Substitution: The Future of Conti Granulation?



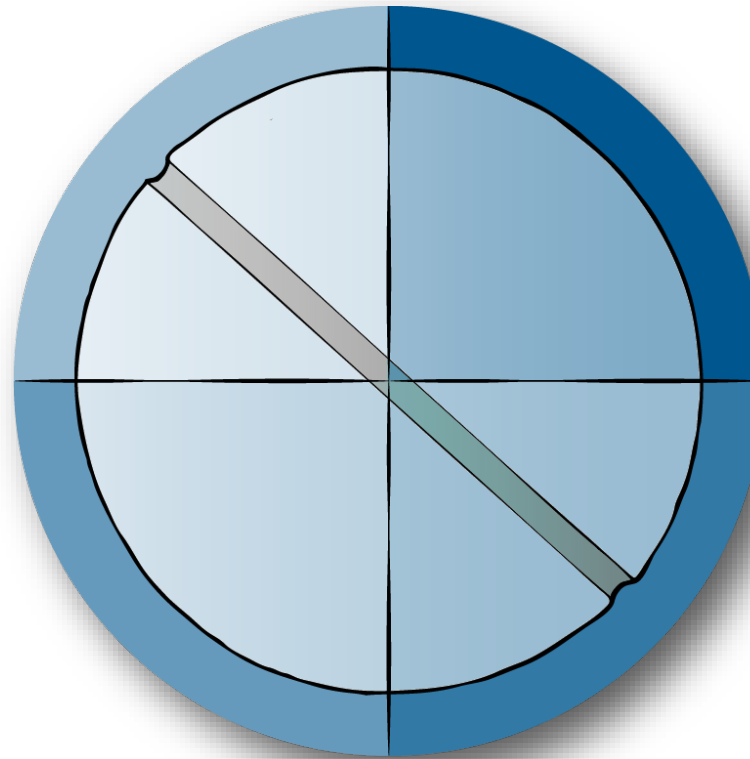
Sources: Pfizer; Quadro/IDEX presentation & information gathered during recent conferences by RS



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Competitive arena

CM Landscape

ConsiGma 25™ – Milestones to product leadership



Continuous
Wet Granulation

CTL 25, 50, 100
Continuous Tableting Line

ConsiGma1
R&D Machine

ConsiGma CDC50
Direct Compression

ConsiGma
Coater



2005

2006

2007

2008

2009

2010

2011

2012

2013

2014

2015

2016

2017

More than 50 references - 2 Continuous Processing test centers (Belgium & USA)

ConsiGma 25™; Vertex Boston (US)



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The Most Important New Drug Of 2012

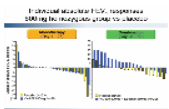
11 comments, 6 called-out [+ Comment Now](#) [+ Follow Comments](#)

The Food and Drug Administration looks set for a great 2012; with a few days left to go, it has approved 40 new drugs and vaccines, one of the most impressive totals ever, according to data from Pharmaceutical Approvals Monthly and FDA press releases. In this haul, one medicine stands out for its scientific and medical importance.



Ten Lessons On Fighting Disease From Michael J. Fox

Matthew Herper
Forbes Staff



The Best Argument That Vertex's CF Drug Combination Works

Matthew Herper
Forbes Staff

Battleground Vertex

Matthew Herper
Forbes Staff

Vertex shares have fallen 37% from their high earlier this year because of doubts by investors that Vertex will succeed in its attempts to dramatically expand Kalydeco's use by combining it with a second drug that will make it work in CF patients whose disease is caused by other, more common, mutations. Initial results were very promising, but then Vertex had to restate them. Sales of its best-seller, Incivek for hepatitis C, are dropping. But whatever you think of Vertex shares, Kalydeco is already a success, with \$113 million in sales in the first nine months of 2012.

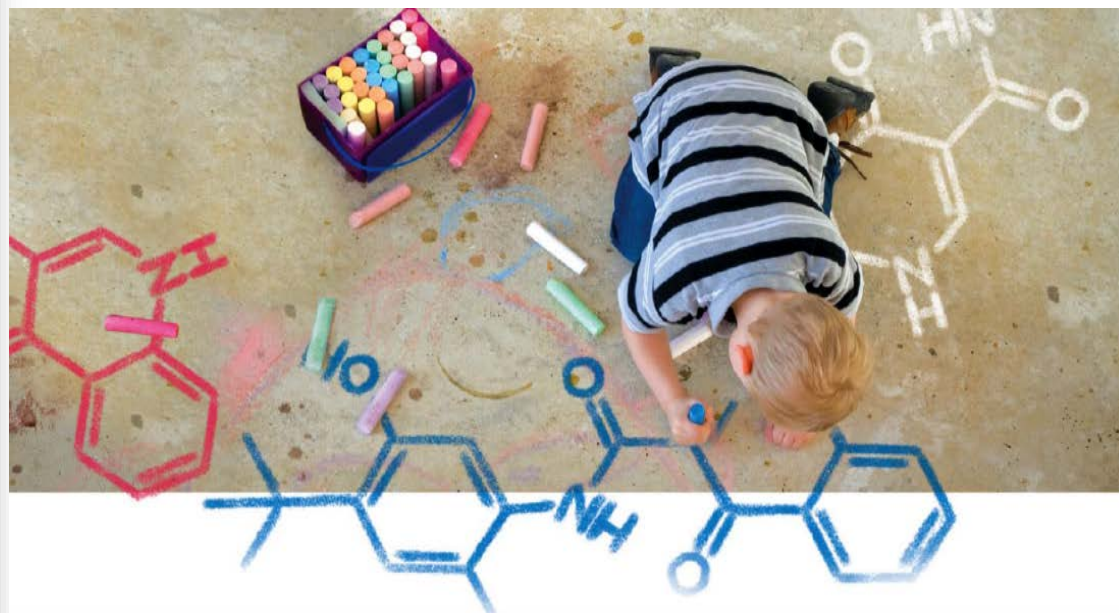
Kalydeco was not the only important drug this year, in which the FDA also approved the first flu vaccine made in cells, not chicken eggs (that's a Novartis product) and several important cancer drugs including Onyx's Kypriolis, Medivation's Xtandi, and Roche's Perjeta. Nor is it the most commercially important — that honor goes to Gilead's Stribild combination pill for HIV, which could help preserve that company's HIV franchise through patent expirations. But it's probably the most exciting as a harbinger of drugs to come.

Kalydeco, for cystic fibrosis, is a triumph of genetics and drug development, the first medicine to directly affect the genetic defect that causes the disease. It will only help 4% of the 70,000 people who suffer from declining lung function, damaged pancreases, and shortened lives due to CF worldwide, but in those few it has a dramatic effect. It makes medical history for three reasons:

- **It's a genomics triumph:** Francis Collins, later famous for heading the Human Genome Project and then the National Institutes of Health, discovered the gene that, when mutated, causes cystic fibrosis 23 years ago. Kalydeco is the first drug to directly affect the defects caused by these mutations, leading to improvements in patients' lung function.
- **A patient group powered its development:** Kalydeco would probably not exist were it not for the Cystic Fibrosis Foundation, which funded its early development at Vertex and gets a royalty on the drug. This success paved the way for other disease foundations including the Michael J. Fox Foundation, Myelin Repair, and the Multiple Myeloma Research Foundation.
- **Its price:** Kalydeco, given alone, will only help a few thousand patients the world over. Like other drugs for very rare diseases, its price is very high: \$294,000 per patient per year.

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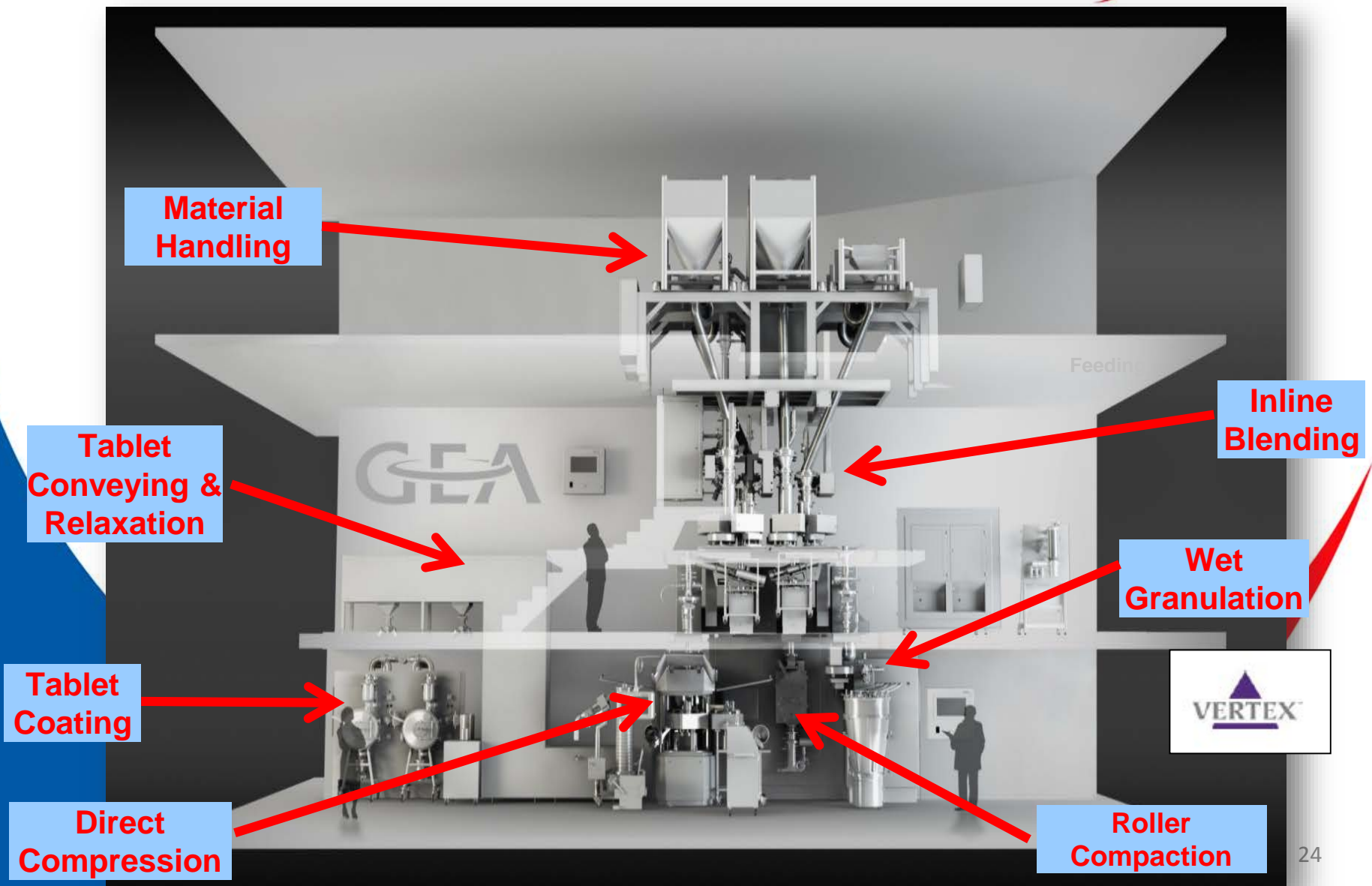


Continuous Processing – GMP Manufacturing Principles and DP Development Strategy

ConsiGma 25™; Vertex Boston (US)



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ConsiGma 25™ PCMM – Pfizer Groton (USA)

in-Pharma
Technologist.com

Pfizer teams with GEA and G-CON to 'transform' oral solid dose industry

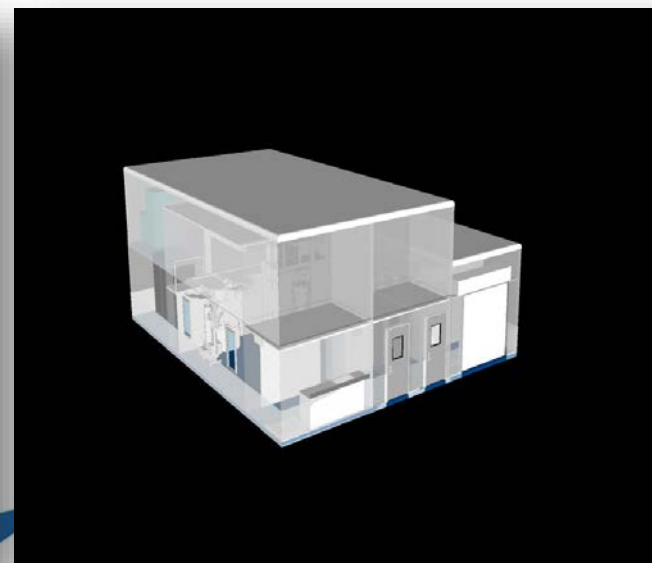
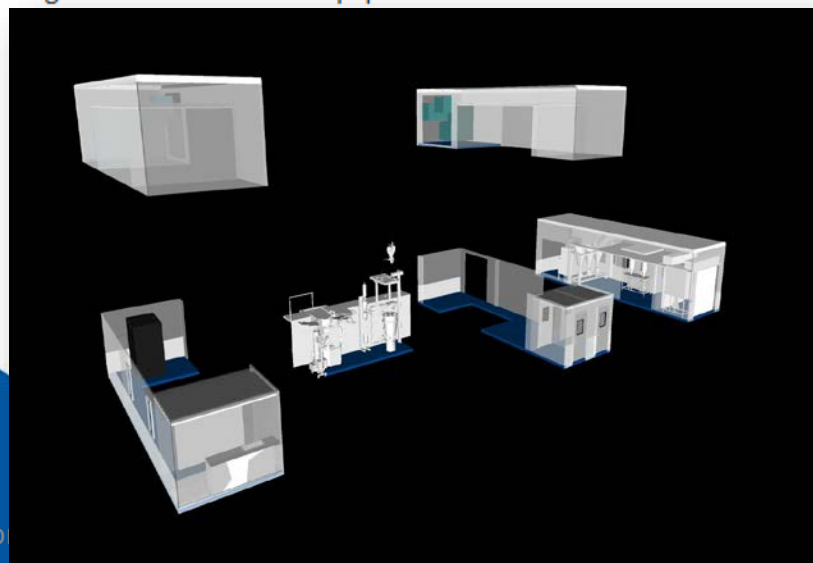
By Dan Stanton+, 26-Sep-2013

A collaboration to develop portable, flexible and continuous processing systems has the potential to transform oral solid dose (OSD) manufacturing, according to Pfizer, GEA and G-CON.

The three companies have formed a PCMM (Portable Continuous Miniature & Modular) joint venture to develop a new oral solid dose processing platform, bringing an innovative and cost-effective approach to traditional manufacturing facilities with fixed equipment and limited flexibility.



Collaboration could transform oral solid dose processing



PCMM paradigm – a change in the pharma industry



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CDC & CDB

GCU

WG & CDB

ConsiGma 25™ PCMM – Pfizer Groton (USA)



Организаторы



Государственный институт
лекарственных средств
и надлежащих практик



Партнеры

Генеральный партнер



Официальный партнер



Партнер конференции



Партнер конференции



Партнер конференции



Партнер сессии



Партнер сессии

