OSD Forms Baseline Guide

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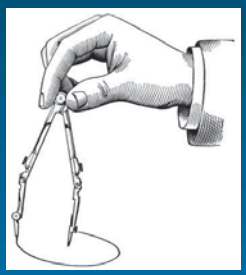
ISPE OSD Baseline Guide

- Professional guidance to global pharmaceutical industry that provides acceptable practice guidance tool in design and developing OSD facilities
- Provides a good guidance as starting point for industry professionals
- Delivers an acceptable practice for achieving regulatory compliance



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Benefit from the ISPE OSD Baseline Guide

Intended to be used by various industry professionals for:

- Business Development
- Manufacturing Ops & Quality Management
- Regulatory Agencies, Inspectors & Auditors
- Science, Technology, Arch & Engineering
- Warehousing/Distribution

1st edition	2nd edition	3rd edition
1998	2009	2016

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Volume 3 Rewrite - Team

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Volume 3 Rewrite - Team

Big Phm	Generic	CMO	A&E	Equip	Ached	US	EU	ASIA	INDIA

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3rd Edition Progressive Outlines

Update Proposal & Initial Plan

June 2013

Team finalization, agreement and Rewrites

Nov 2013-July2014

Final Edits/GDC Reviews 4Q2015 (progress)

Officially Kicked off **Nov 2013**

Annual Meeting

Industry Review and Revisions **Aug 2014-Jan 2015**

Industry Available Release **1Q2016**

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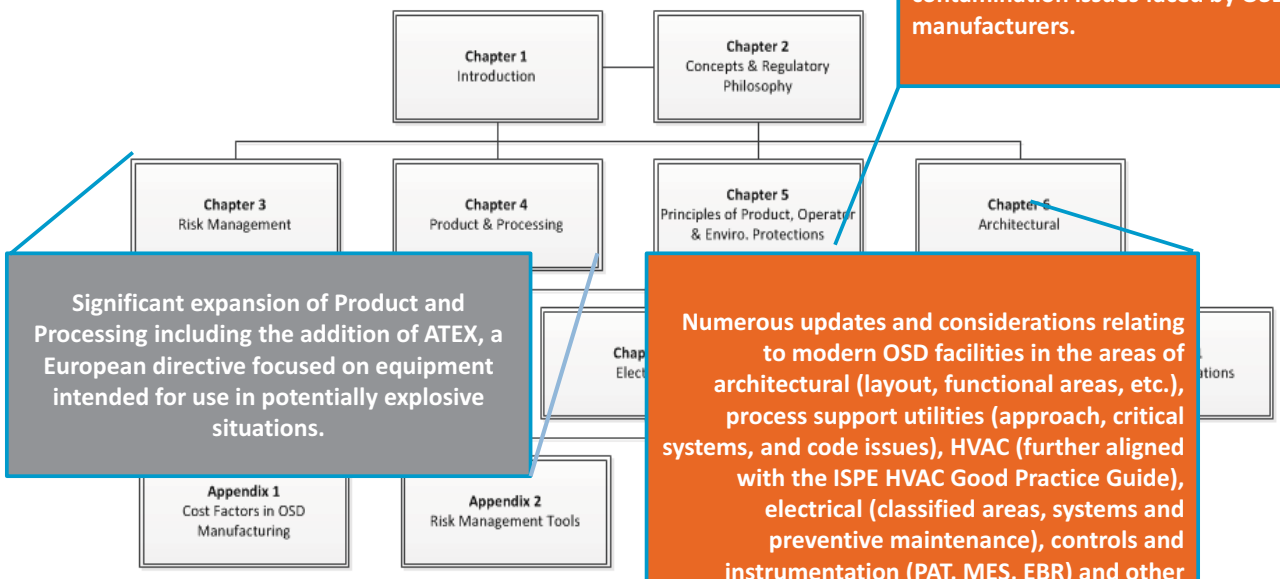
Content and Revisions

New chapter that goes into more detail on the challenges, issues and considerations relating to containment and cross contamination issues faced by OSD manufacturers.



Significant expansion of Product and Processing including the addition of ATEX, a European directive focused on equipment intended for use in potentially explosive situations.

Numerous updates and considerations relating to modern OSD facilities in the areas of architectural (layout, functional areas, etc.), process support utilities (approach, critical systems, and code issues), HVAC (further aligned with the ISPE HVAC Good Practice Guide), electrical (classified areas, systems and preventive maintenance), controls and instrumentation (PAT, MES, EBR) and other considerations (non-cGMP risks, exposure, life/safety, hazardous operations, environmental, emergency preparedness).

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Content and Revisions

- Revised the structure for better flow and communication
- Increased coverage of process technologies
- Risk Based Approach
- Incorporate with EU and JP standards and regulations, e.g. ATEX
- Quality by Design (QdB)
- Product Quality Lifecycle Implementation (PQLI)

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OSD BG3 - Highlights

- Expanded discussion related to Risk Management (Chapter 3) with content including the topics of: Principles, Processes and Applicable Tools.
- Significant expansion of Product and Processing (Chapter 4) including the addition of "ATmospheric EXplosible (ATEX)", a European directive focused on equipment intended for use in potentially explosive situations.

- New chapter entitled **Product Isolation and containment - Principles of Product, Operator, and environmental Protection.**
  - Detail on the challenges, and considerations relating to containment and cross contamination issues inOSD manufacturers

Quality by Design (QdB)

Aligned with ICH regulatory guideline Q8R2 as:

A systematic approach to development that begins with predefined objectives and emphasizes product and process understanding and process control, based on sound science and quality risk management

Key to Success

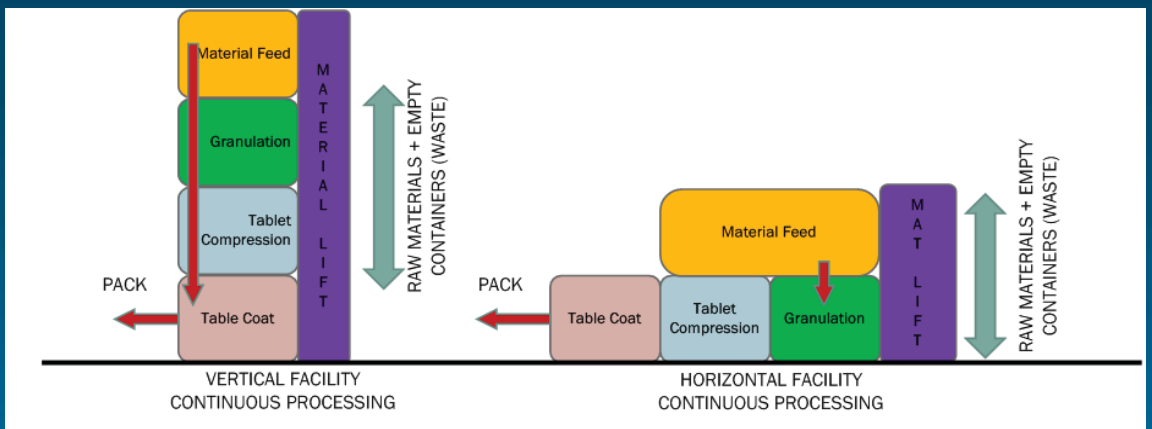
Process and Process Development

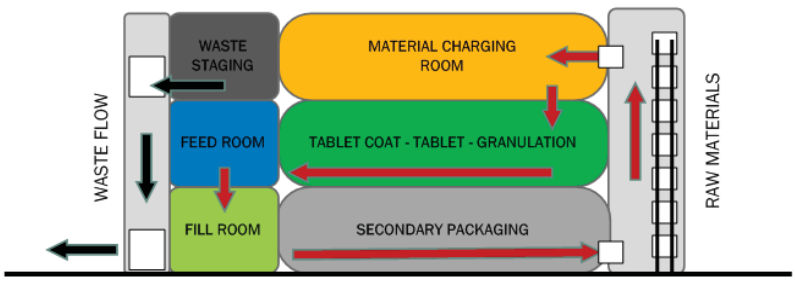
Protection by Design: Product, Process, Personal and Environment

Facility Layout, Critical Utility Criteria and Facility Equipment Configuration

Fit-in-use; Time-valued-Investment; Technological-Advancement

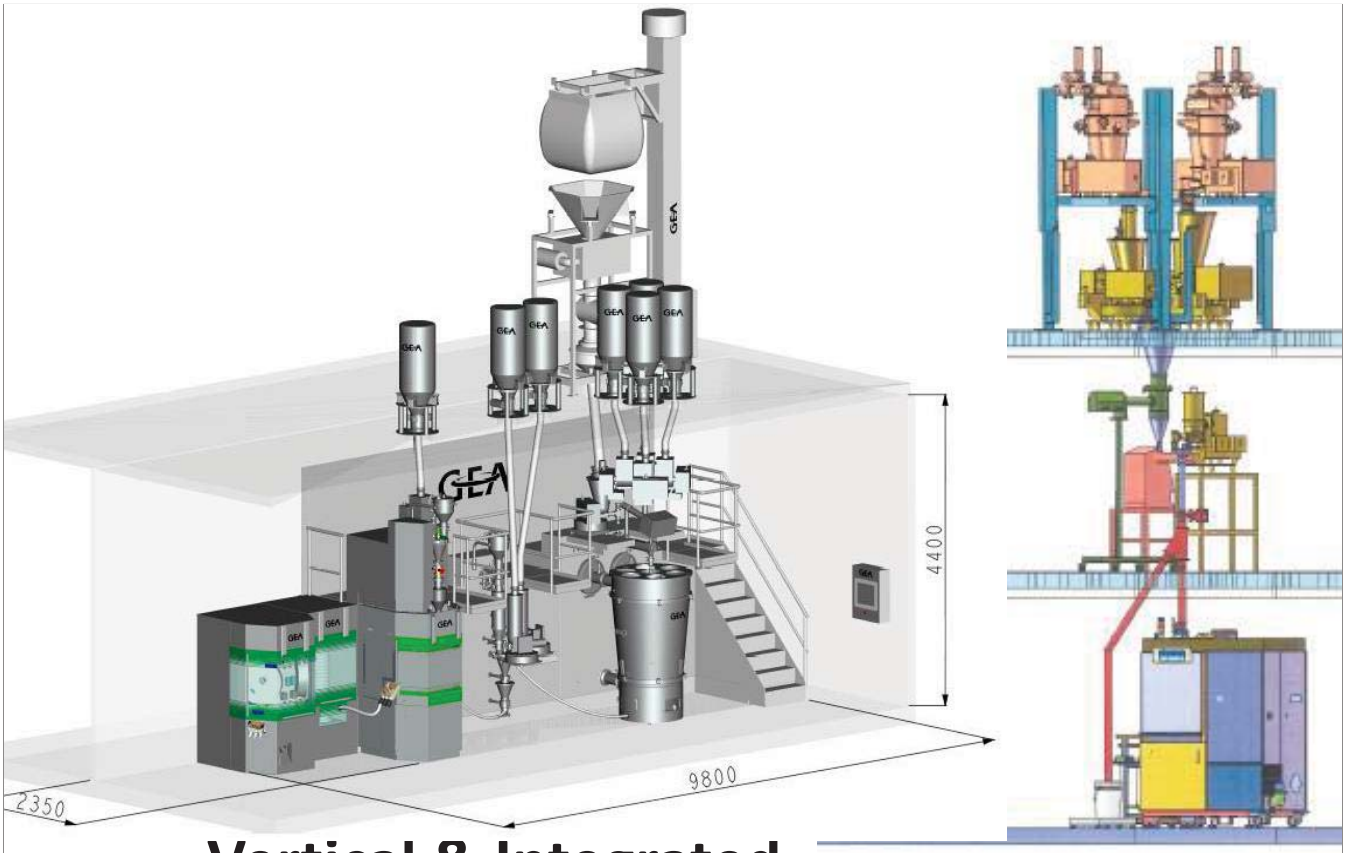
Facility Layout Comparison





FULLY INTEGRATED FACILITY WITH HORIZONTAL GRANULATION FLOW FOR CONTINUOUS PROCESSING

Conceptual Future Continuous Manufacturing with Robotic Warehouse



Vertical & Integrated Process

Benefits

Create more capable and capabilities in the global marketplace:

- Introduction of facility models which are:
  - smaller
  - more energy efficient
  - less wasteful
  - Opportunities for increasing productive
  - significantly less costly to build and operate
  - reduced WIP (Work In Progress) space and material
- Improves the quality control for consistency
- Decrease scale up issues and tech-transfer cycle time

Enable for faster launching of new products

Opportunity for reduction of Full-Time-Equivalents and increasing of OEE

PAT and CMP

The way of our future Pharmaceutical Manufacturing Operations

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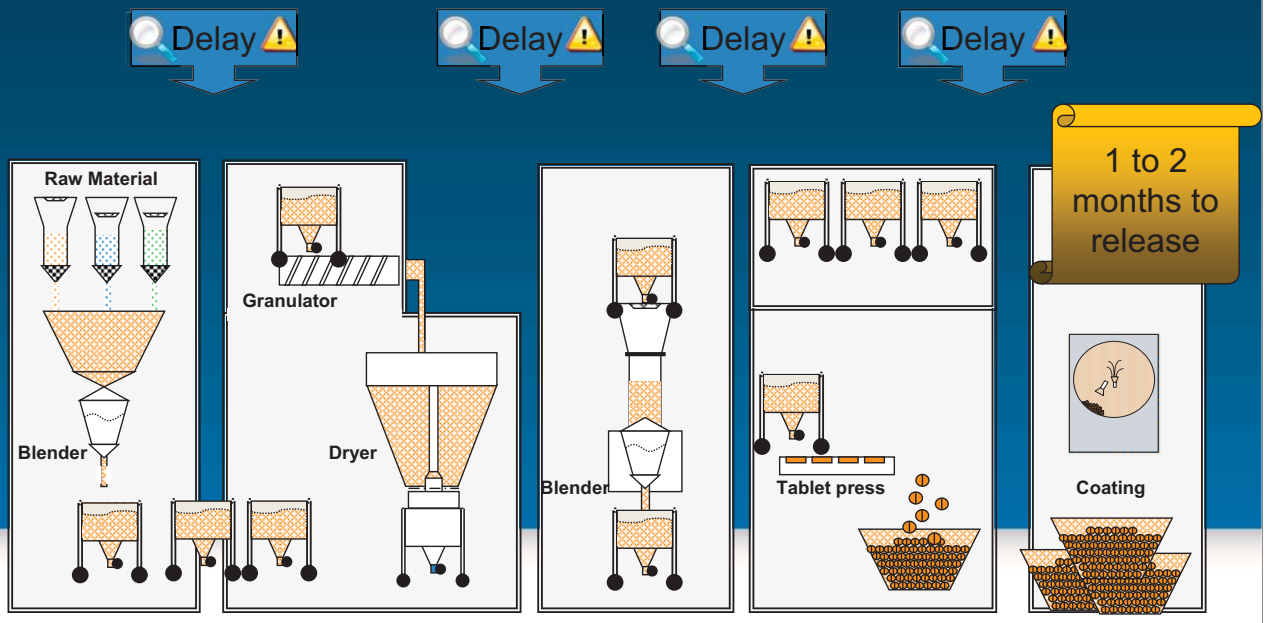
Oral Solid Dosage today



High inventory including “work in progress”, long changeovers, disconnected processes, high process losses, off line analysis, low asset utilization, …

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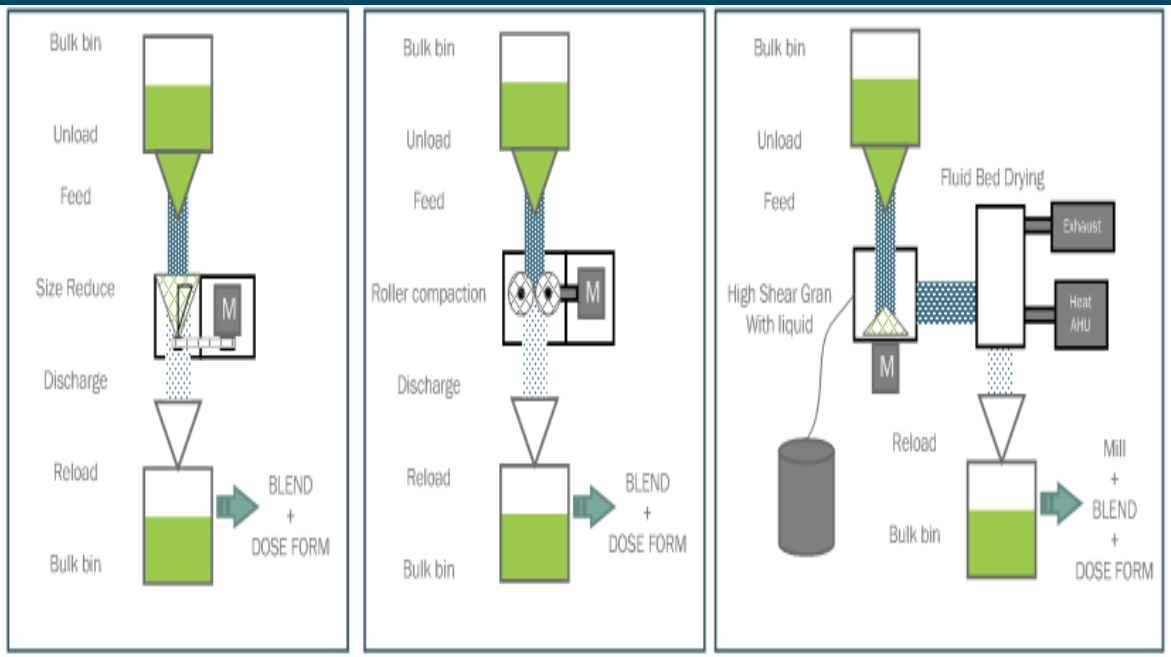
Granulation Processes Review

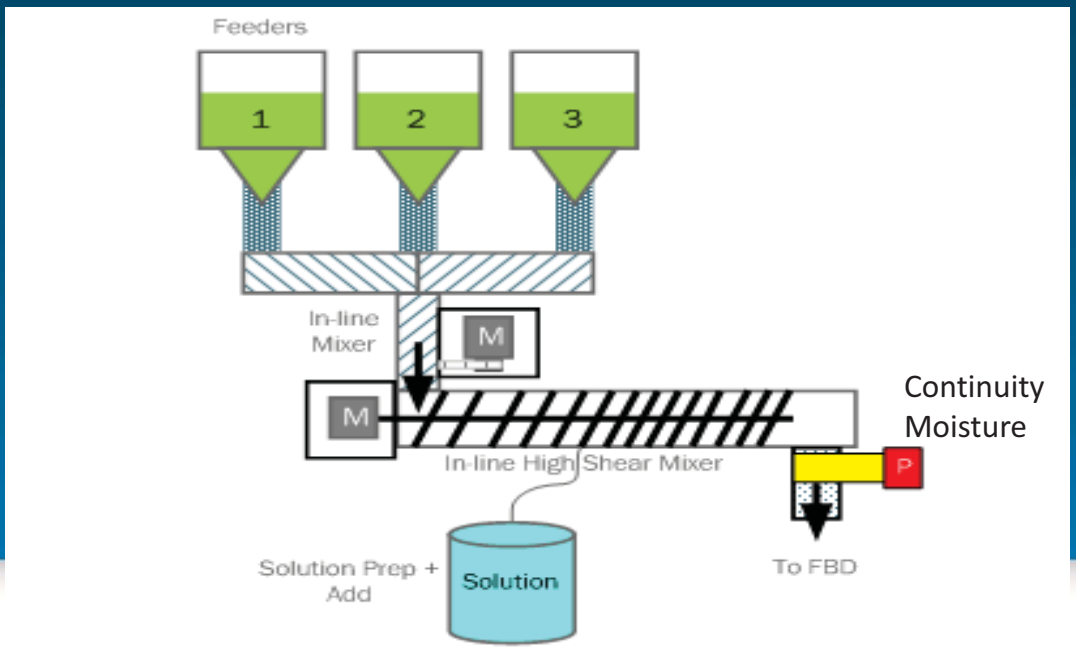


DIRECT COMPRESSION DRY GRANULATION WET GRANULATION

Designs compatible with Continuous Operations

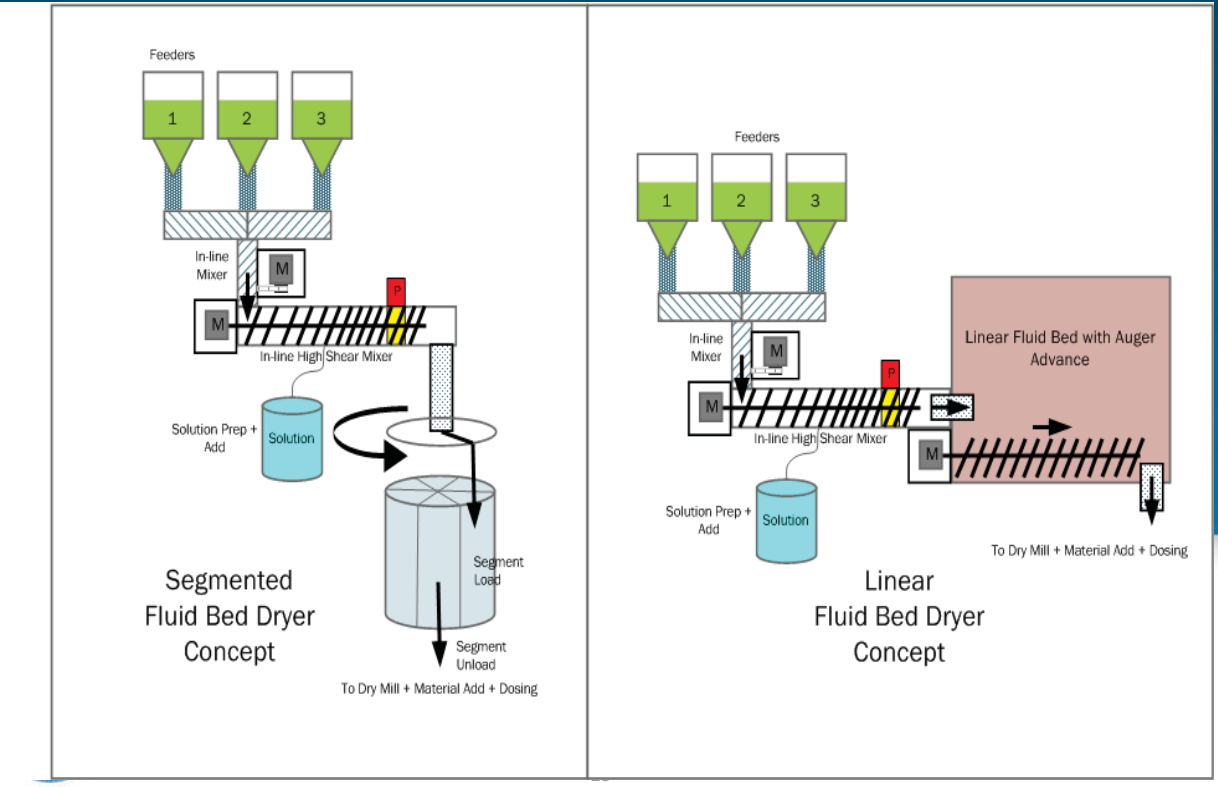
Batch by Nature

Continuous Processing
In- Line Granulation

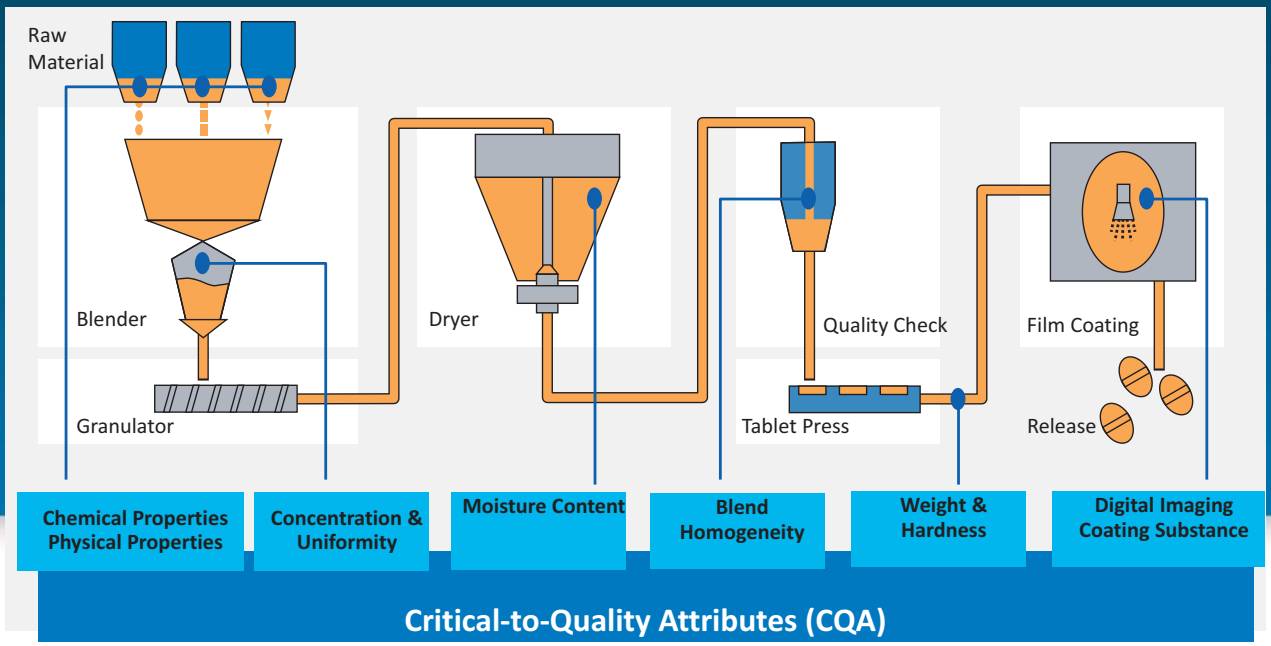


IN-LINE HIGH SHEAR GRANULATOR

Continuous Processing
Fluid Bed Dryer Concepts



What to Understand: Product CQA and Process Control Requirements



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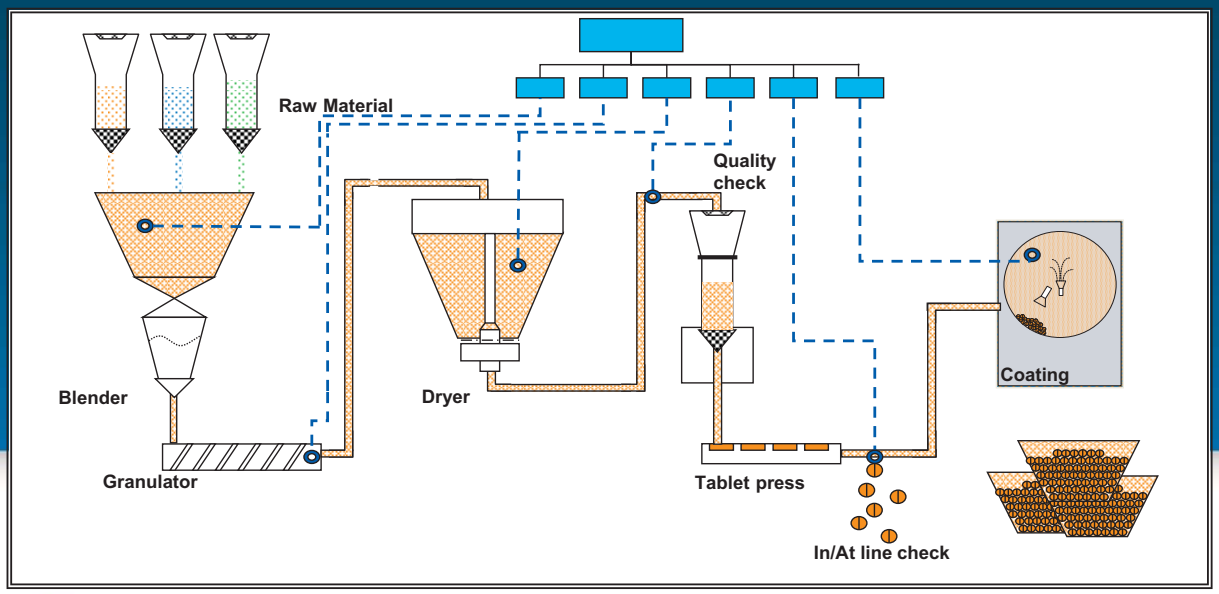
What to Control: PAT Quality Data Management System



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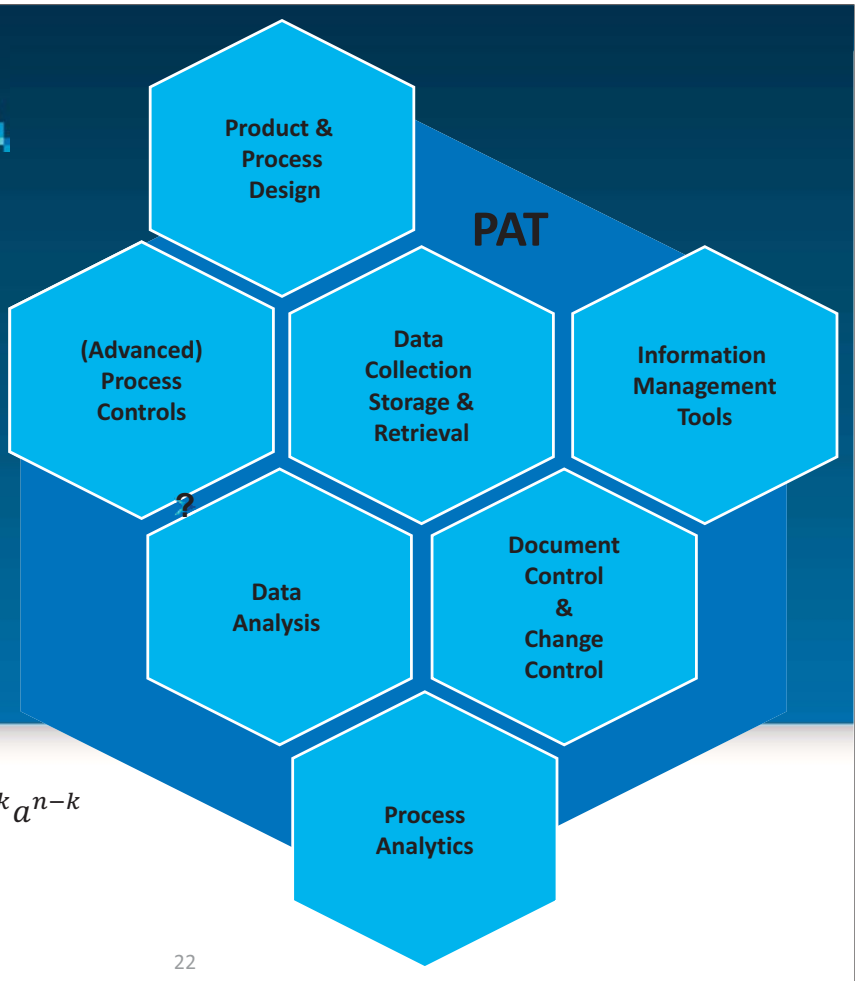
PAT?



$$(x+a)^n = \sum_{k=0}^{n} \binom{n}{k} x^k a^{n-k}$$

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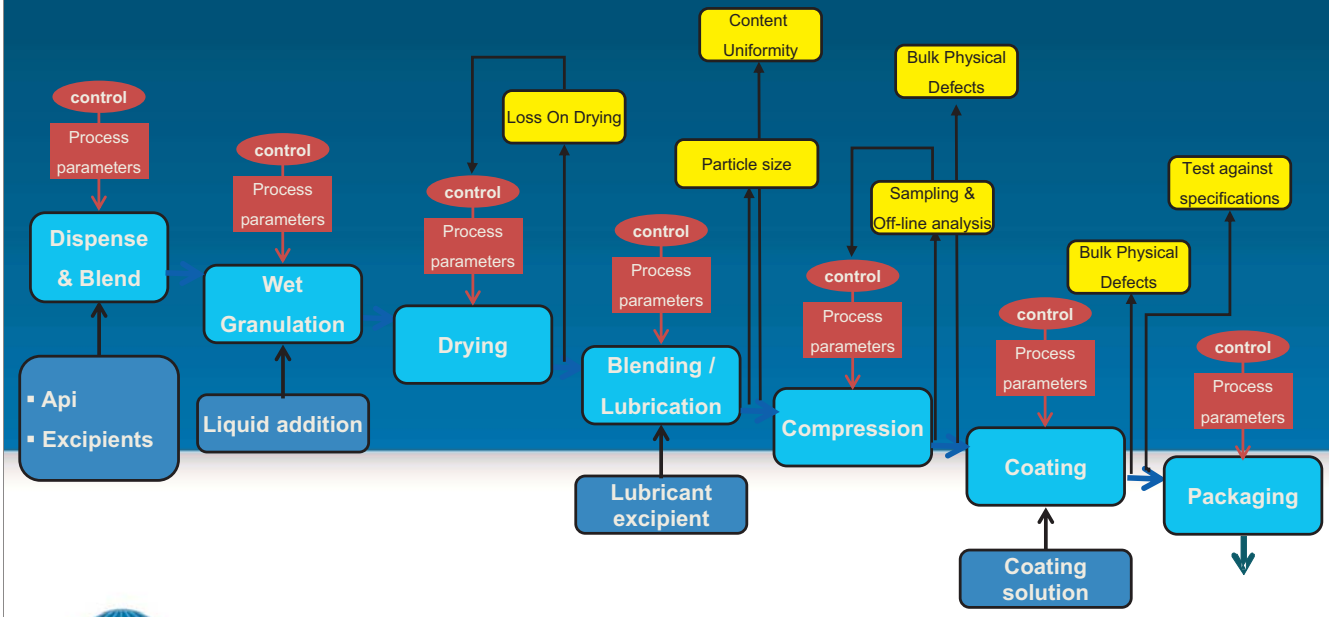
PAT in Solid Dosage



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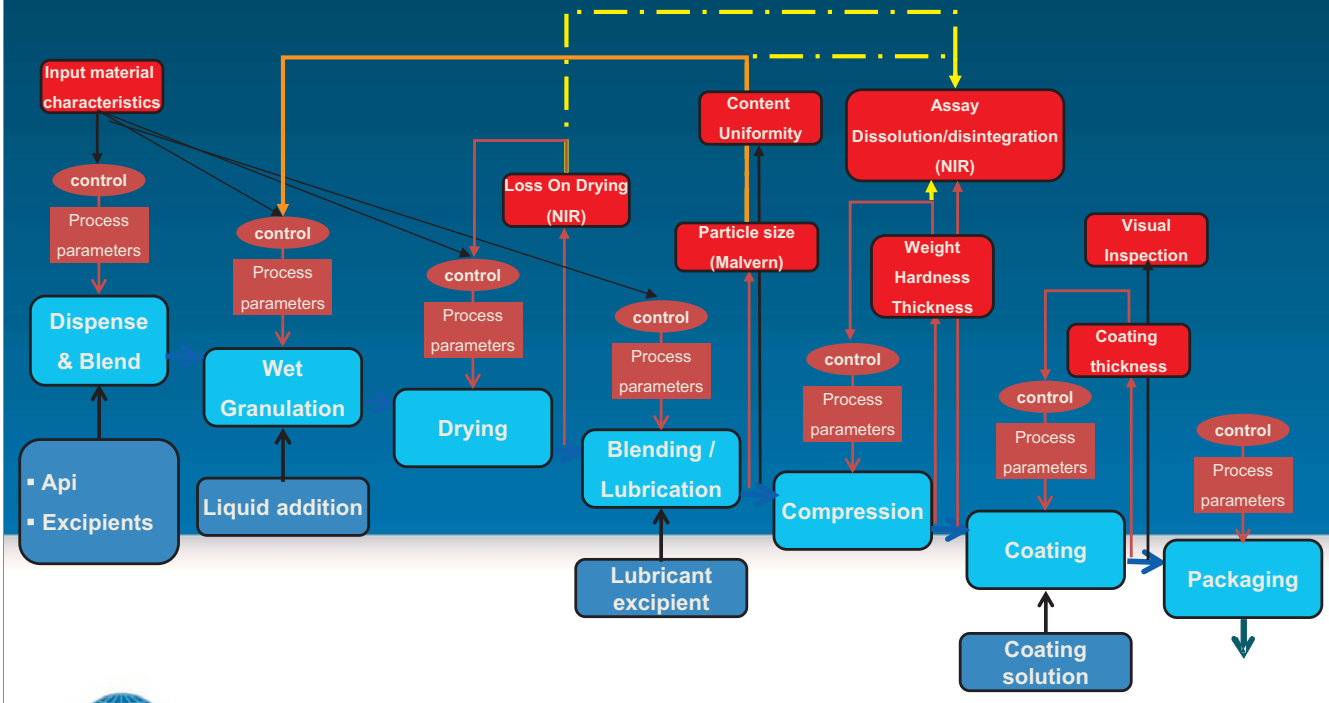

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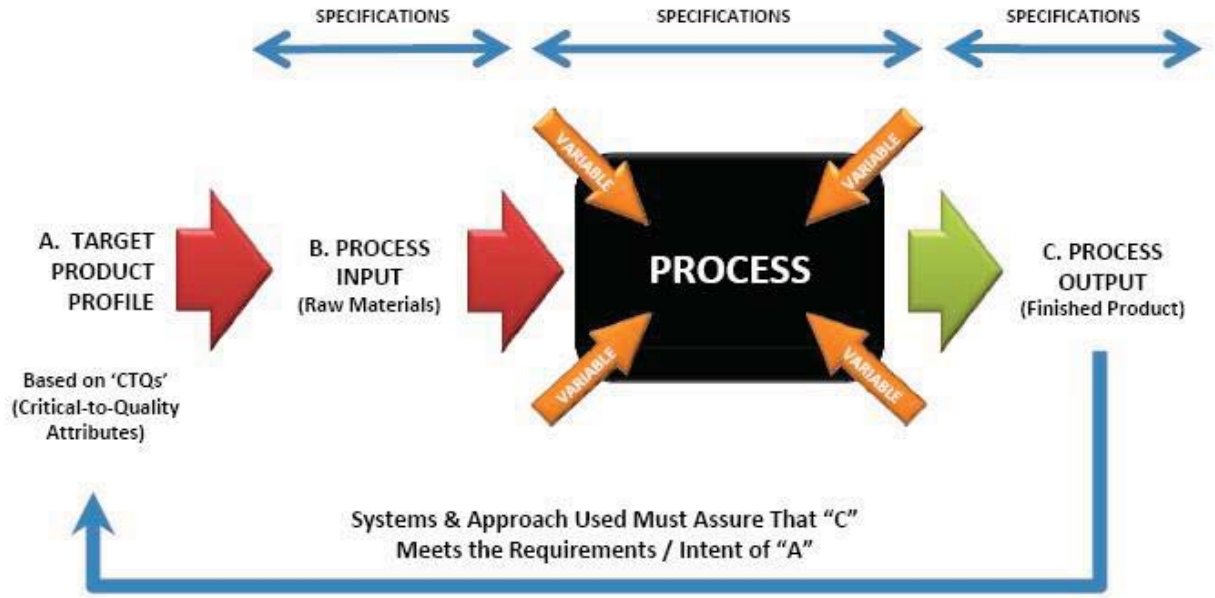
CQA to CPP – the Specification



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Efficiency

- Processes will require less Foot-Prints, less Initial-Capital
- Operation could be continuous for 24/7
  - Fewer startup/shutdown quality problems
  - 100% capacity utilization (OEE)
- Closed Operation with Fully Automated Systems
  - Less Human Intervention; Less operator exposure to product
  - Less Exposure to Environment; Less Exposure of Cross-Contamination to Product
- Just-in-time operation minimizes the product storage and in-process quarantine

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Source: Duquesnes University

Statistical Data Suggests

- **Continuous Manufacturing** must be aligned with **PAT**
  - **Reduced scrap/rework**
  - **Reduced human errors**
  - **Increased & consistent product quality**
  - **Reduced quality costs**
  - **Reduced regulatory compliance costs**
  - **Faster time to market: scale-up & tech transfer**
  - **Real-time product release**

- **The future is not a million miles away; it is here, in Boston Area!**

Thank you!