



9th ADVANCED GMP WORKSHOP 2024

Achieving Operational Excellence through Continuous Manufacturing

Presented By
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Global Chief Manufacturing Officer
Cipla Ltd.

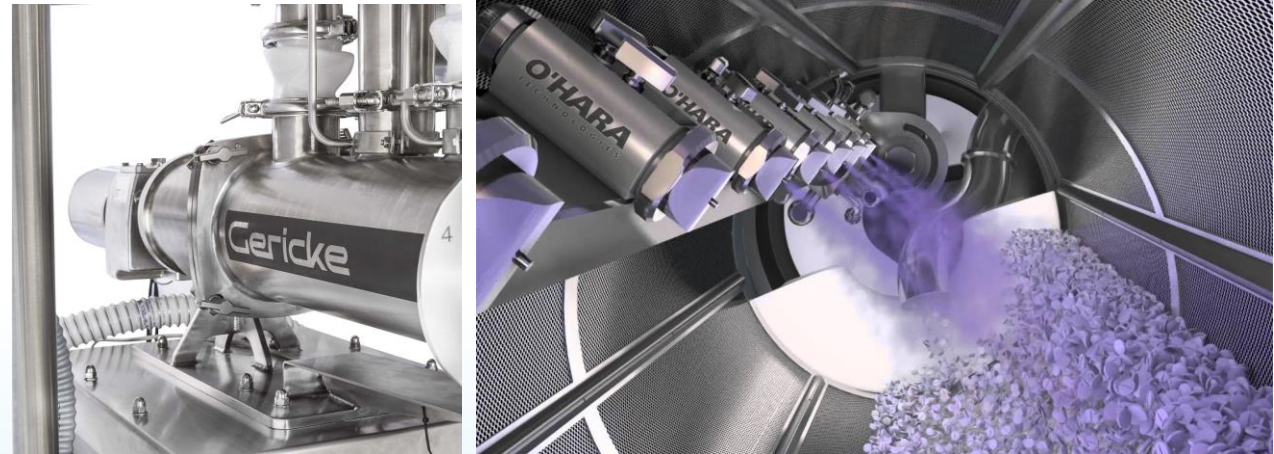
Cipla has successfully explored hybrid CM pathway for both API & Formulations...

Active Pharmaceutical Ingredients



Journey Started : 2018
Commercial Readiness : 2 Products

Formulations Operations

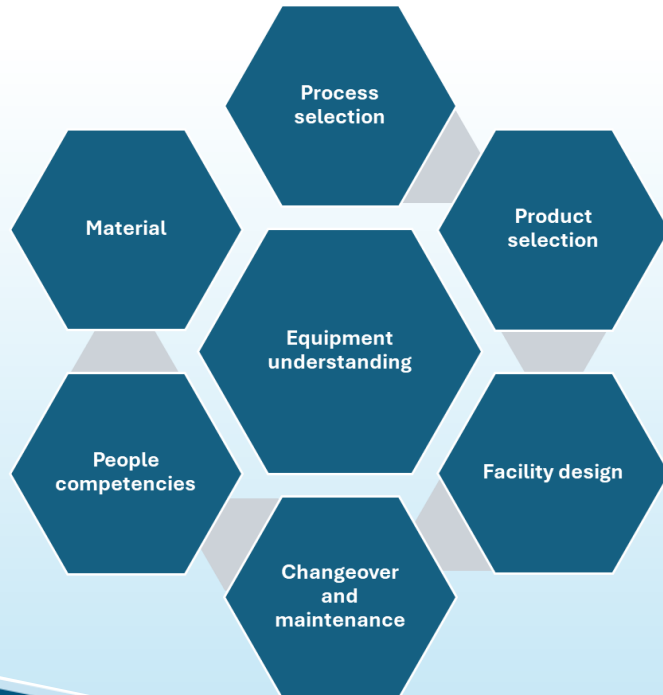


Journey Started : 2023
Commercial Readiness : 2 Products

All Project Goals Delivered

- ✓ Integrated Processing with Fewer Steps; Shorter process times, Higher Efficiencies; Increased Safety
- ✓ Reduced Cost ; Smaller Facility & Equipment; Reduced inventory / WIP; Flexible Operations;
- ✓ Online monitoring and control for increased product quality assurance in real time; consistent quality

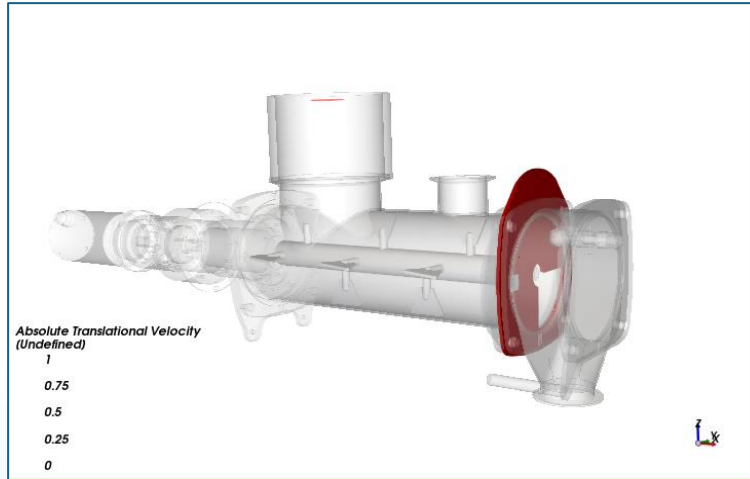
...success can be attributed to careful considerations across the seven elements...



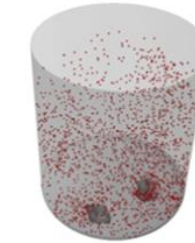
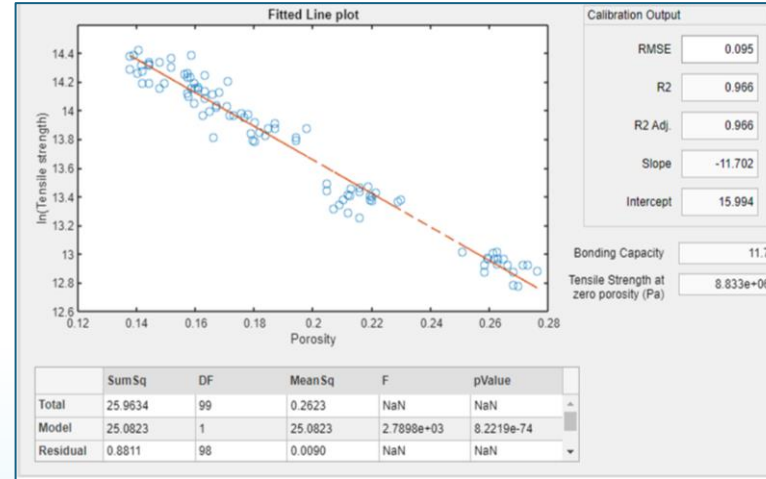
1. **Process Selection** : Dry Granulation [Process of Choice]
2. **Product Selection** : # of Material [Cont. Blender] ; Volume & Robustness
3. **Materials** : Excellent flow properties
4. **Facility** : Mixed – Blending & compression – Vertical; Coating - Horizontal
5. **Equipment Understanding** : Pilot of Continuous Blender
6. **People Competencies** : Focused Team; Technology & Digital Skills
7. **Changeover & Maintenance** : Training ; Standardization for changeover

... and leveraging Digital Twin for Critical Unit Operations Optimization.

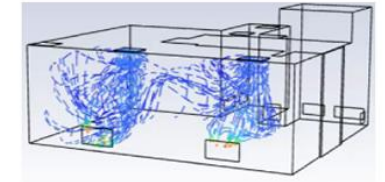
DEM Simulation of CM Line



Digital Twin for Formulation evaluation



Digital Twin of Suspension Mixing



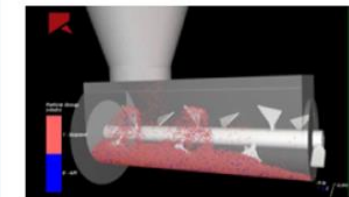
Digital Twin of Clean Room



Digital Twin of Roll Compaction



Digital Twin of Compression



Digital Twin of Continuous Blender



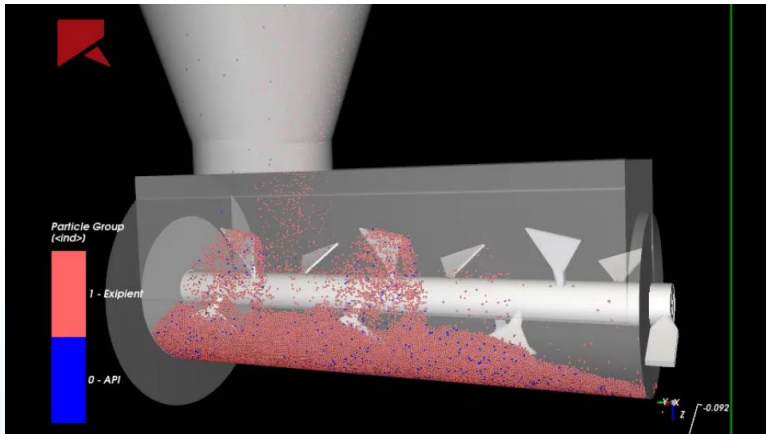
Digital Twin of Fluidized Bed Granulator

- Discrete Element Method used for Creating Digital Twin
- Assisted in understanding and performance evaluation of New Equipment

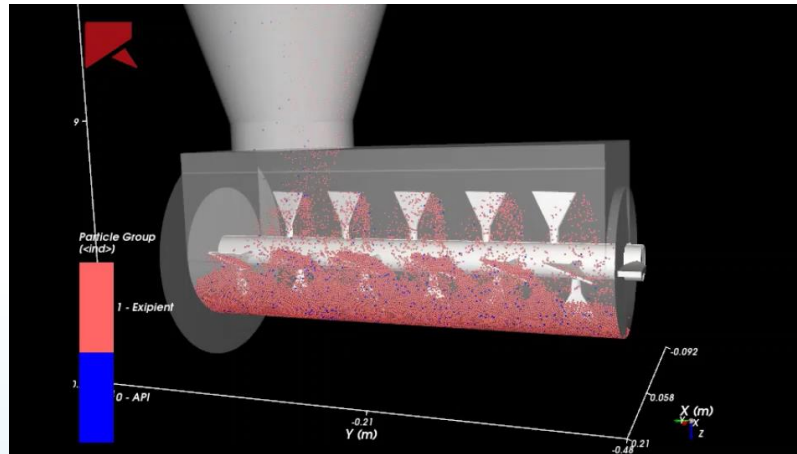
- Mechanistic Model for Insilico Formulation assessment for CM line
- Insilico studies resulted in improved performance and throughput

Leveraged Digital Twin for Insilco Continuous Blending Process Development ...

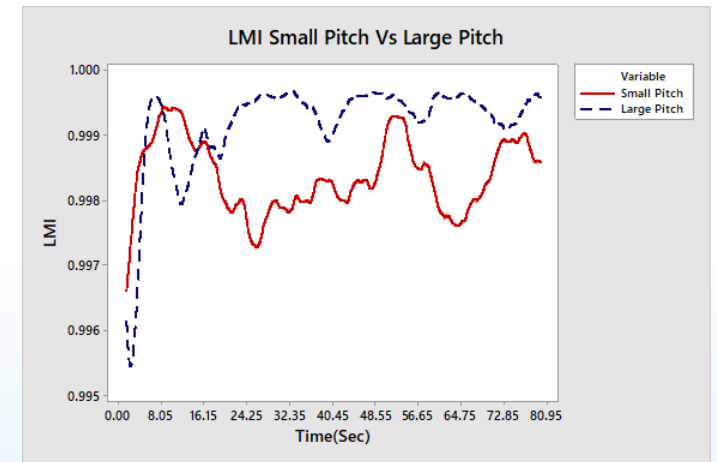
Large pitch Blender



Small Pitch Blender

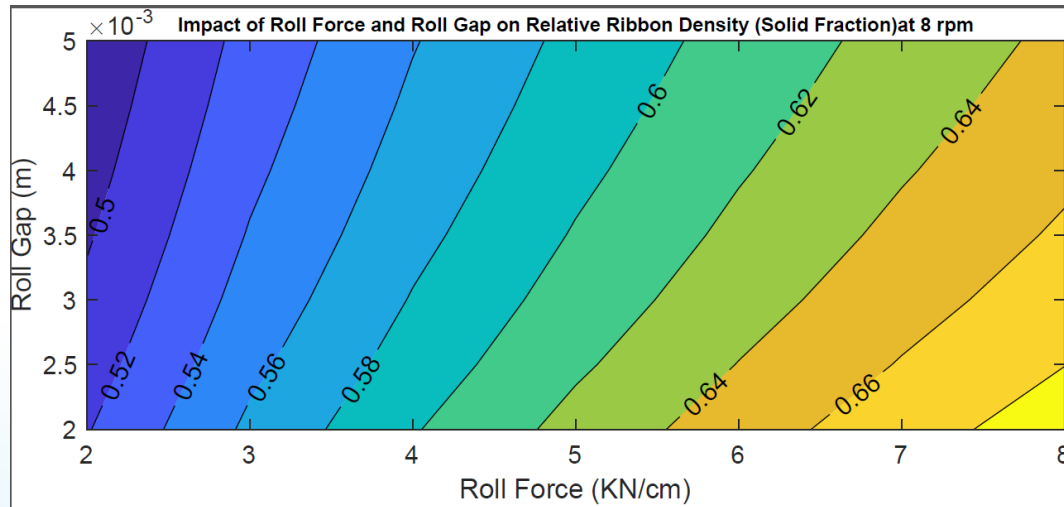


Mixing Index

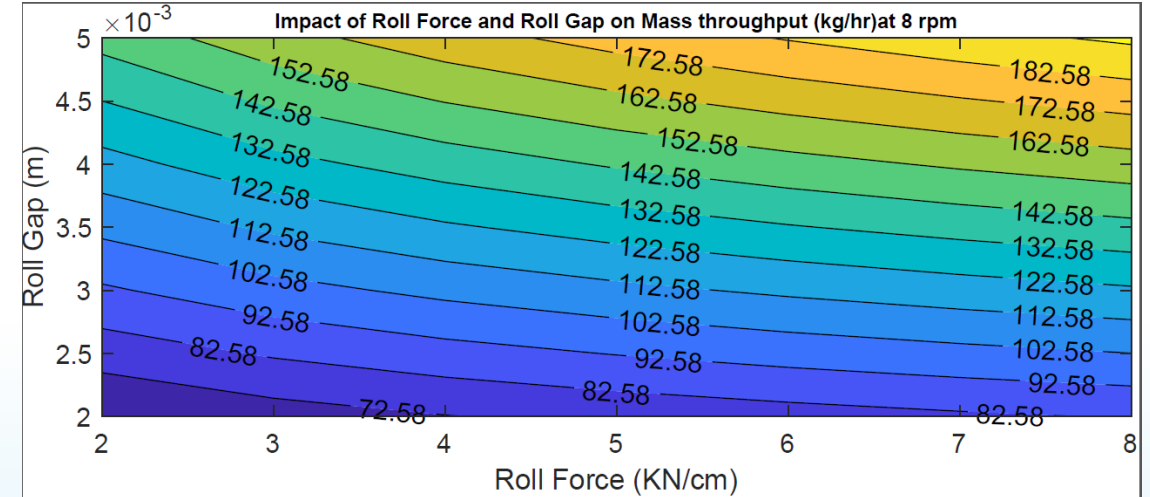


- Insilco Simulations : Avoided the cost of ordering the two blenders saving time & money
- Simulations demonstrated that large pitch blender will provide better mixing than small pitch blender
- Insilco Process Design started even before arrival of the Physical equipment saving time

... and Insilco Roll Compaction Process Development optimizing design spaces...



Insilco Design Space for Granule Quality



Insilco Design Space for Throughput Maximization

- Digital Twin of Roll Compaction developed
- The Twin created Insilco Design Space which helps
 - In Identifying the right parameters to get granules of good quality
 - Maximizing Throughput without taking trials

... delivering the Formulations Continuous Manufacturing Project Objectives successfully.

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50%

Reduction
Dispense to Dispatch
Time

35%

Reduction
Extent of
Touch

83%

Reduction
Cost INR per '000
Tablets

80%

Reduction
Manufacturing
Footprint

PAT

Blend & Content
uniformity Real-time
assurance and release

Checkmaster

Weight , Hardness, Thickness
with auto feedback
control

Thank You