

# Advanced Manufacturing Apprenticeship



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# Before Pfizer



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# During Pfizer



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# End Point Assessment



*SIAS*



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# Now (Continuous Manufacturing)

## Introduction

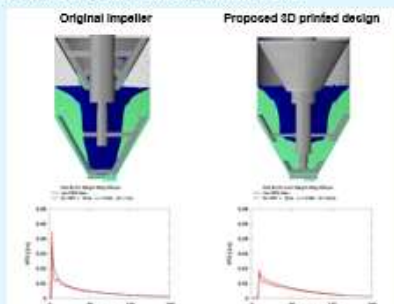
- The Sandwich CMT facility has been operational since December 2017
- The facility is designed to be flexible to integrate various unit operation eg. **blending**, **direct compression**; **twin screw wet granulation**, and **encapsulation**.
- This development facility has allowed rapid execution of numerous work packages over the last 18 months. Some highlights are:
  - ❖ **Glasdegib** process understanding to support the filing document
  - ❖ PCMM Default formulation development with **Dacomitinib** to aid the choice of formulations
  - ❖ Process start up procedures optimisation to support JAK1 campaigns
  - ❖ CMT Design space process understanding: residence time distributions (RTD), low and high throughput levels (10-30 kg/h)



## From the digital world with DEM

### Problem Statement

- At high impeller rotation speeds centrifugal force pushes materials towards the wall and creates void in the CMT that result in material by-passing the mixer.
- DEM process simulation were performed with new impeller designs to visualise the powder movement in the CMT.



## To the real world with 3D printing

### Rapid Prototyping

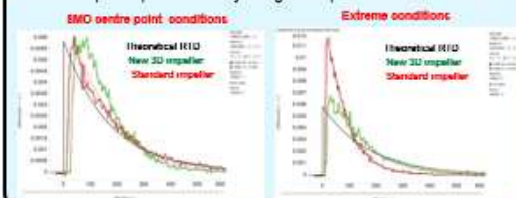
- Based on DEM simulations results a concept impeller was selected for the new impeller (picture below).
- This concept design was then produced by 3D printed in Groton to allow for testing in the Sandwich CMT.
- From concept to physical impeller took ~ 2 weeks.



## DEM validation with experiments

### Results

- Successful trials were conducted with the 3D printed impeller using placebo formulation.
- Residence time distribution curves of this new impeller were obtained at various process conditions.
- Experimental results are consistent with simulations where bypass behaviour of the CMT was eliminated.
- The new impeller design expanded the CMT operating space and allows operation with conditions that were previously challenging.
- Next step is to print the newly designed impeller in stainless steel.



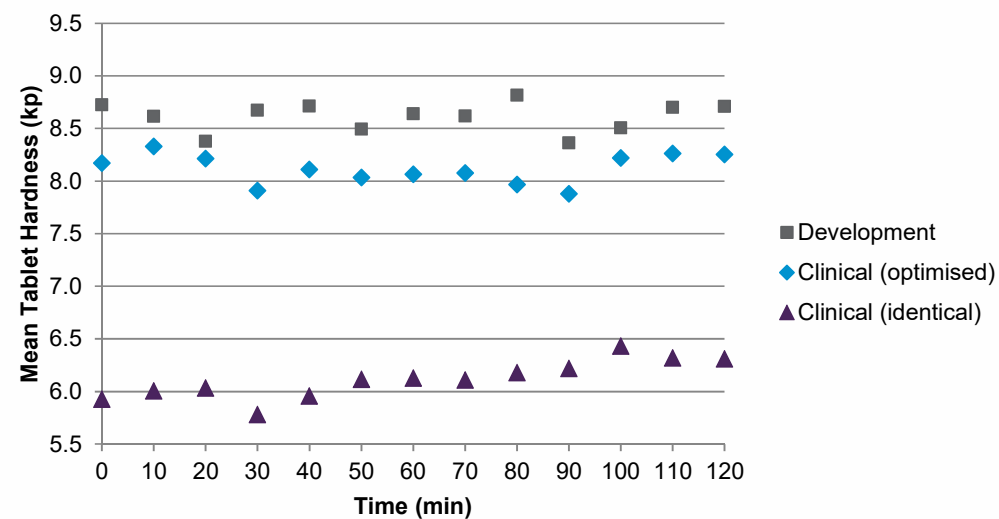
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# Now (Tablet Press Comparison)



Compression force (kN)		Hardness (kP)		Tensile strength (MPa)		Solid Fraction		Compression stress (MPa)	
Clinical	Dev	Clinical	Dev	Clinical	Dev	Clinical	Dev	Clinical	Dev
2.0	2.0	3.46	1.60	0.593	0.241	0.624	0.462	39.79	39.79
3.0	3.0	6.39	4.81	1.233	0.878	0.689	0.532	59.68	59.68
4.0	4.0	9.01	7.04	1.865	1.366	0.737	0.557	79.58	79.58
5.0	5.0	11.68	9.81	2.566	2.059	0.770	0.591	99.47	99.47
6.0	6.0	14.37	12.56	3.323	2.786	0.803	0.615	119.37	119.37
8.0	8.0	18.54	17.17	4.548	4.084	0.846	0.643	159.15	159.15
10.0	10.0	21.88	21.00	5.527	5.270	0.872	0.664	198.94	198.94
11.9	11.9	23.86	24.80	6.195	6.395	0.893	0.678	236.74	236.74



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