POSTER 61

# The CMAC MicroFactory: Mefenamic Acid

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## Aims

To prepare mefenamic acid particles of two sizes for *in vitro* testing

## Wet milling

## Crystallisation

## Isolation

## Performance testing

**Seed generation:**

- Mefenamic acid (MFA) in heptane
- Milled for 90 min at 26k rpm using fine rotor
- MFA solid loading: 4.62 wt%

| Particle size (μm) | |
|---|---|
| D10 | 12.5 |
| D50 | 27.3 |
| D90 | 51.5 |

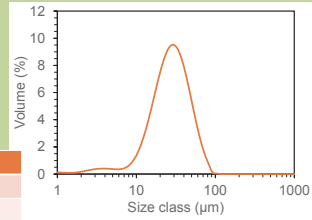



**Figure 1** Malvern Mastersizer particle size distribution.

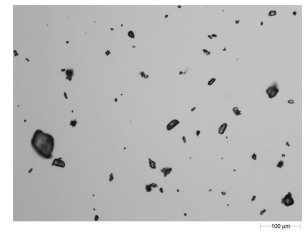
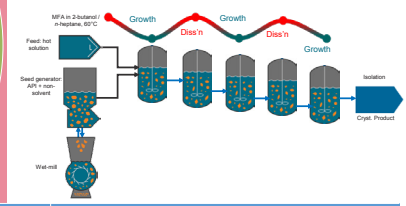


**Figure 2** Malvern Morphologi G3 image of seeds.

**A digital first approach:**
Mechanistic population balance modelling was used to determine the process conditions required to obtain the maximum and minimum particle sizes for a fixed vessel configuration.

### Targeting maximum size (D50 = 125 μm)




| | Mean temperature (°C) | | | | |
|---|---|---|---|---|---|
| | Stage 1 | Stage 2 | Stage 3 | Stage 4 | Stage 5 |
| Model | 20.0 | 60.0 | 20.0 | 60.0 | 20.0 |
| Operation | 19.5 | 59.5 | 19.4 | 59.4 | 24.8 |

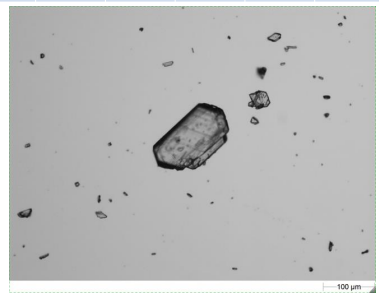
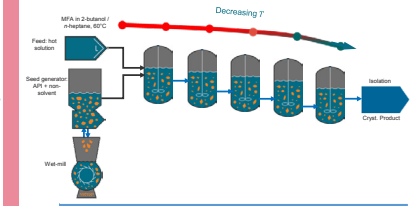


**Figure 3** Malvern Morphologi G3 image of process targeting maximum particle size.

### Targeting minimum size (D50 = 34 μm)




| | Mean temperature (°C) | | | | |
|---|---|---|---|---|---|
| | Stage 1 | Stage 2 | Stage 3 | Stage 4 | Stage 5 |
| | 20.0 | 56.7 | 52.9 | 47.3 | 38.8 |
| | 19.5 | 55.4 | 53.7 | 47.7 | 34.7 |

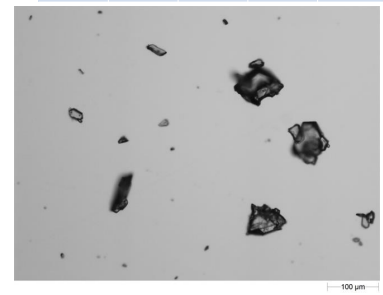


**Figure 4** Malvern Morphologi G3 image of process targeting minimum particle size.

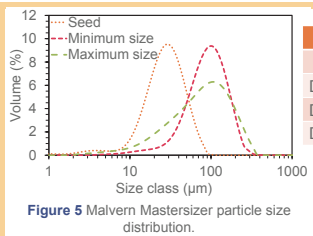



**Figure 5** Malvern Mastersizer particle size distribution.

| Particle size (μm) | | |
|---|---|---|
| | Target: Minimum | Target: Maximum |
| D10 | 40.0 | 20.3 |
| D50 | 91.1 | 79.6 |
| D90 | 171.0 | 194.0 |

**Isolation:**
Analysis of product satisfies British Pharmacopoeia specifications.

**Tablet formulation:**

- 50 % w/w MFA
- Excipients:
  - Avicel PH-101
  - HPMC
  - Ac-di-Sol SD-711-NH
  - GranuLac 230
  - Mg stearate

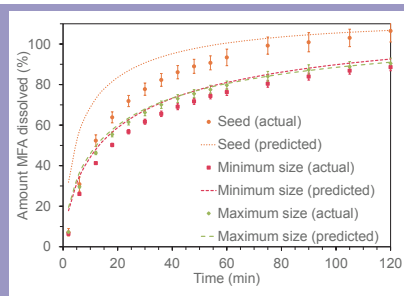



**Figure 6** Actual and predicted dissolution performance.

## Future work

Comparison of open loop control with set points from mechanistic control and closed loop advanced process control

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CMAC Tier 2 partners:

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