In-line Particle Characterization of Fluid Bed Granulation By Parsum

HKI-272 Oct 2009 Campaign at Excella

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Objective

- Study impact of formulation attributes on particle size and distribution

- **Batch/Multiviarate Statistical Process Control (BSPC/MSPC)**
  - Evaluate batch performance
  - Study batch-to-batch variation
Monitor Fluid Bed Granulation/Drying

Critical Unit Operation
Fluid Bed Granulator

In-line monitoring of particle size distribution using Parsum

In-line monitoring of moisture using NIR

In-line monitoring of manufacturability CQAs using process analyzers
### Material and Experimental

- **Equipment:** Aeromatic S3 fluid bed
- **Batch Size:** 30-35Kg

<table>
<thead>
<tr>
<th>Batch</th>
<th>Povidone</th>
<th>MgSt</th>
<th>Disintegrant</th>
</tr>
</thead>
<tbody>
<tr>
<td>0910275</td>
<td>5%</td>
<td>2%</td>
<td>CPV</td>
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<tr>
<td>0910276</td>
<td>5%</td>
<td>2%</td>
<td>CPV</td>
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<tr>
<td>0910426</td>
<td>7.50%</td>
<td>1%</td>
<td>CPV</td>
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<td>0910427</td>
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In-line particle characterization of HKI-272 granulation batches Oct 2009

- Batch 910275
- Batch 910426
- Batch 910441
- Batch 910276
- Batch 910427
- Batch 910442
- Batch 910277
- Batch 910428
- Batch 910443

Probe fouled during batch
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Chordlength x50 increases notably with increasing Povidone
Disintegrant type also appears to affect particle size growth
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Chordlength x10 increases notably with increasing Povidone
Disintegrant type also appears to affect particle size growth
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Chordlength x90 increases notably with increasing Povidone
Disintegrant type also appears to affect particle size growth
Variables included:

Chordlength data (number-based, volume-based), particle rate, particle velocity etc

Each point represents a combination of multiple variables at a particular time point
Variables included:
Chordlength data (number-based, volume-based), particle rate, particle velocity etc

Each point represents a combination of multiple variables at a particular time point
Batch-level Process Modeling

Variables included:
Chordlength data (number-based, volume-based), particle rate, particle velocity etc

Each point represents a batch calculated based on raw data