In-line Particle Characterization of Fluid Bed Granulation By Parsum

HKI-272 Oct 2009 Campaign at Excella

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GMS

Pfizer

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

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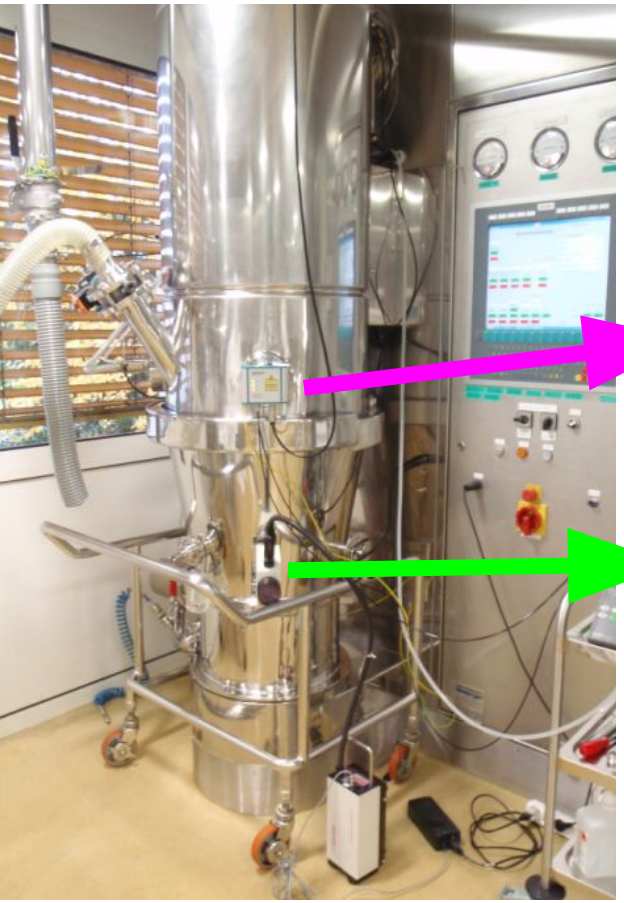
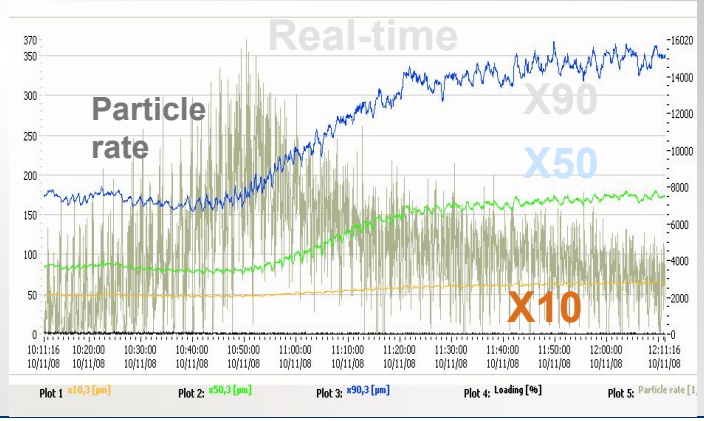
Monitor Fluid Bed Granulation/Drying

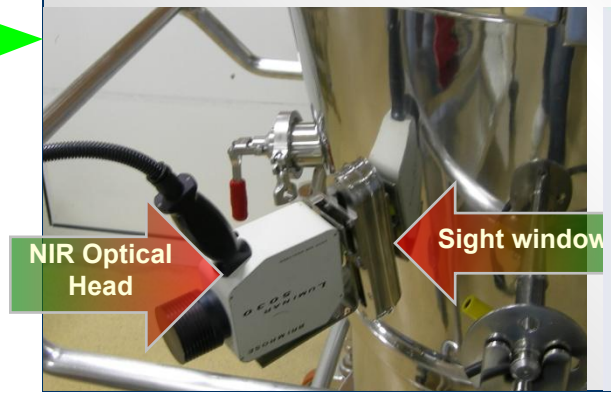
Critical Unit Operation
Fluid Bed Granulator

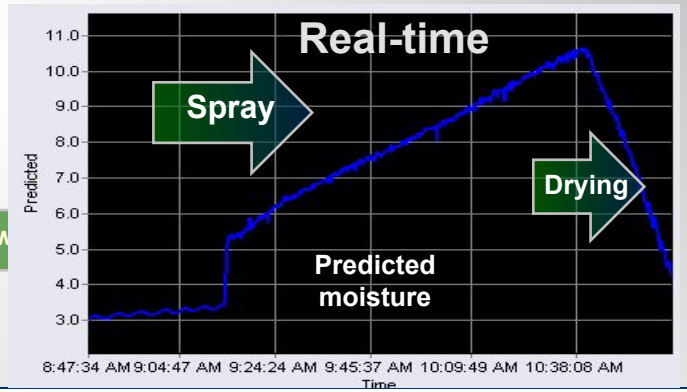


In-line monitoring of particle size distribution using Parsum



In-line monitoring of moisture using NIR





Material and Experimental

Batch	Povidone	MgSt	Disintegrant
0910275	5%	2%	CPV
0910276	5%	2%	CPV
0910277	5%	2%	CPV
0910426	7.50%	1%	CPV
0910427	7.50%	1%	CPV
0910428	7.50%	1%	CPV
0910441	7.50%	1%	CCS
0910442	7.50%	1%	CCS
0910443	7.50%	1%	CCS

Equipment: Aeromatic S3 fluid bed

Batch Size: 30-35Kg

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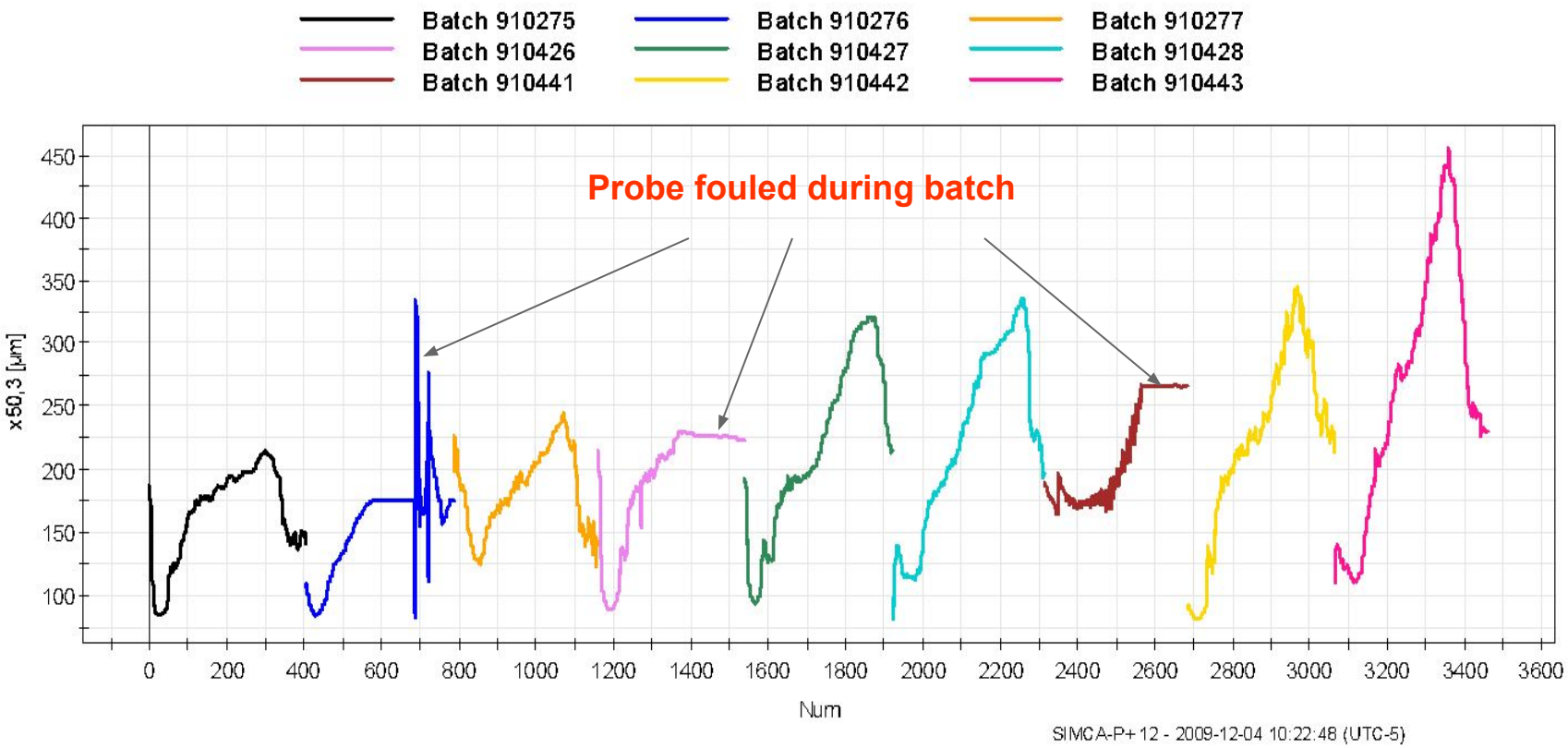
X50 Median

In-line particle characterization of HKI-272 granulation batches Oct 2009



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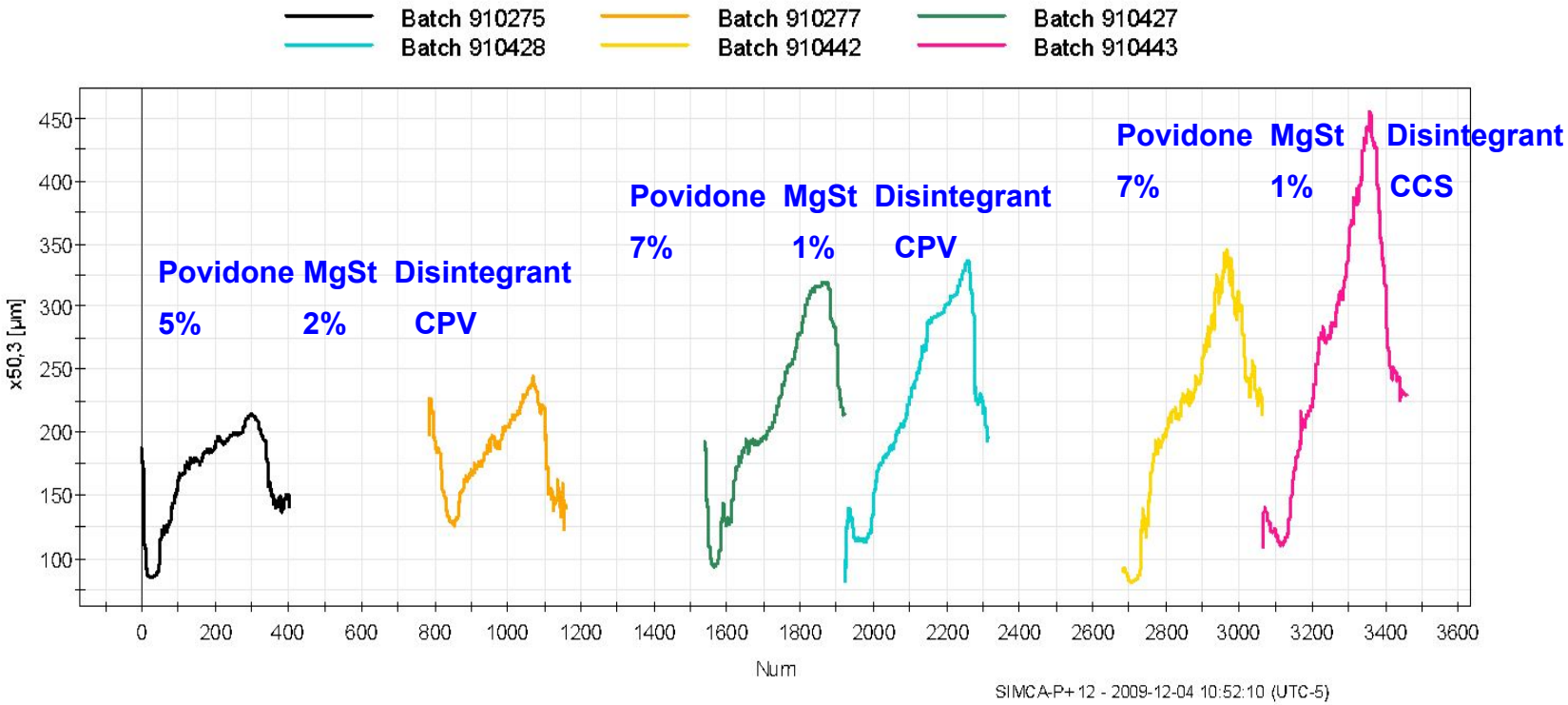
X50 Median

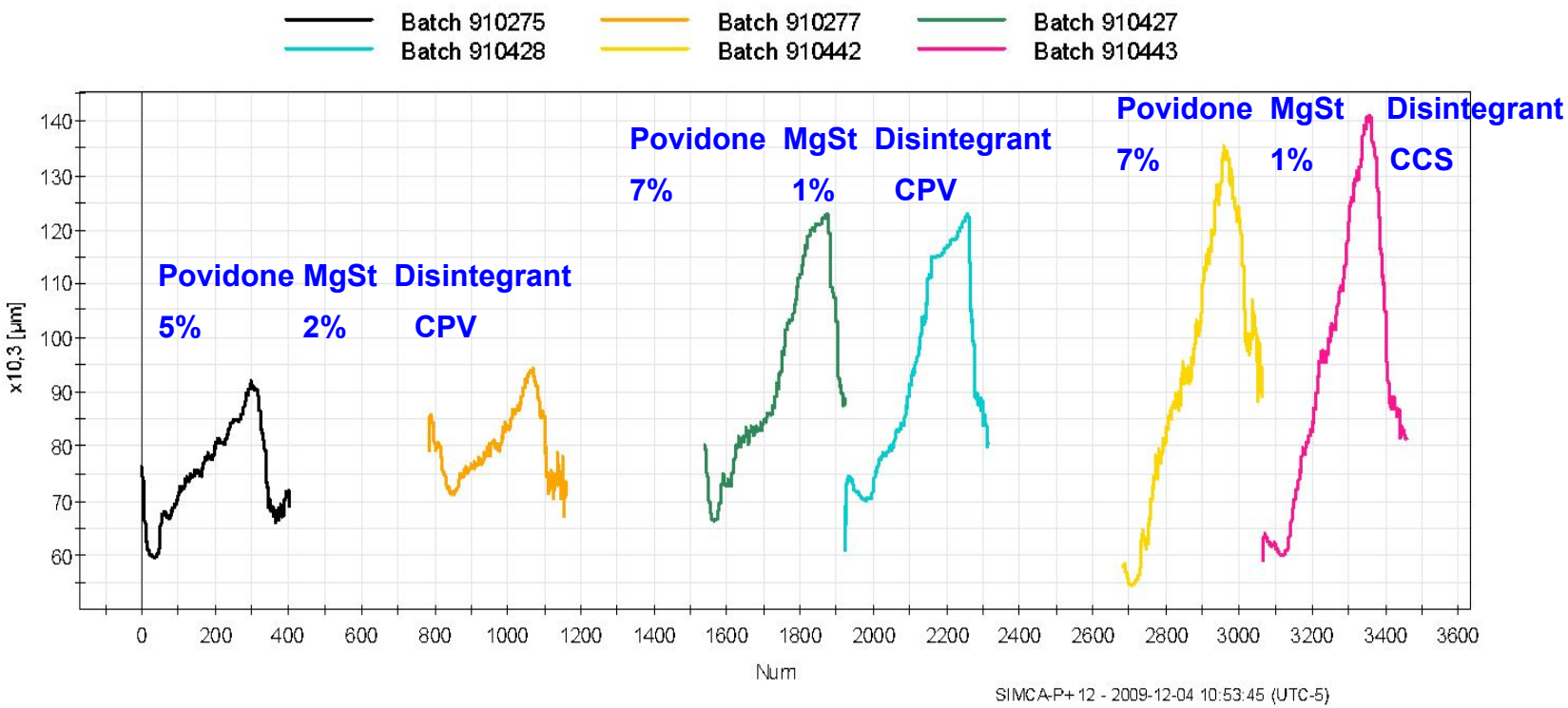
In-line particle characterization of HKI-272 granulation batches Oct 2009



Chordlength x50 increases notably with increasing Povidone

Disintegrant type also appears to affect particle size growth

In-line particle characterization of HKI-272 granulation batches Oct 2009



Chordlength x10 increases notably with increasing Povidone

Disintegrant type also appears to affect particle size growth

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X90

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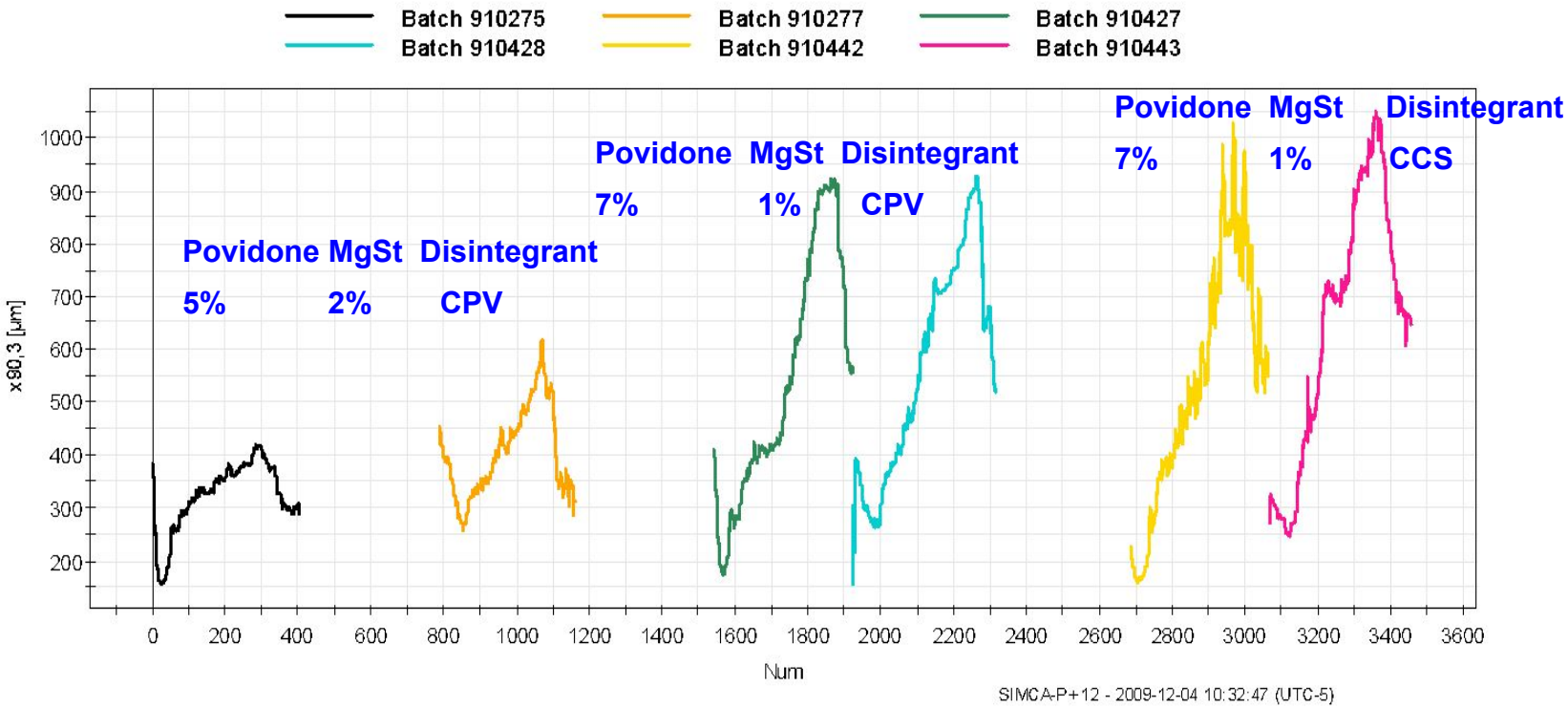

Chordlength x90 increases notably with increasing Povidone

Disintegrant type also appears to affect particle size growth

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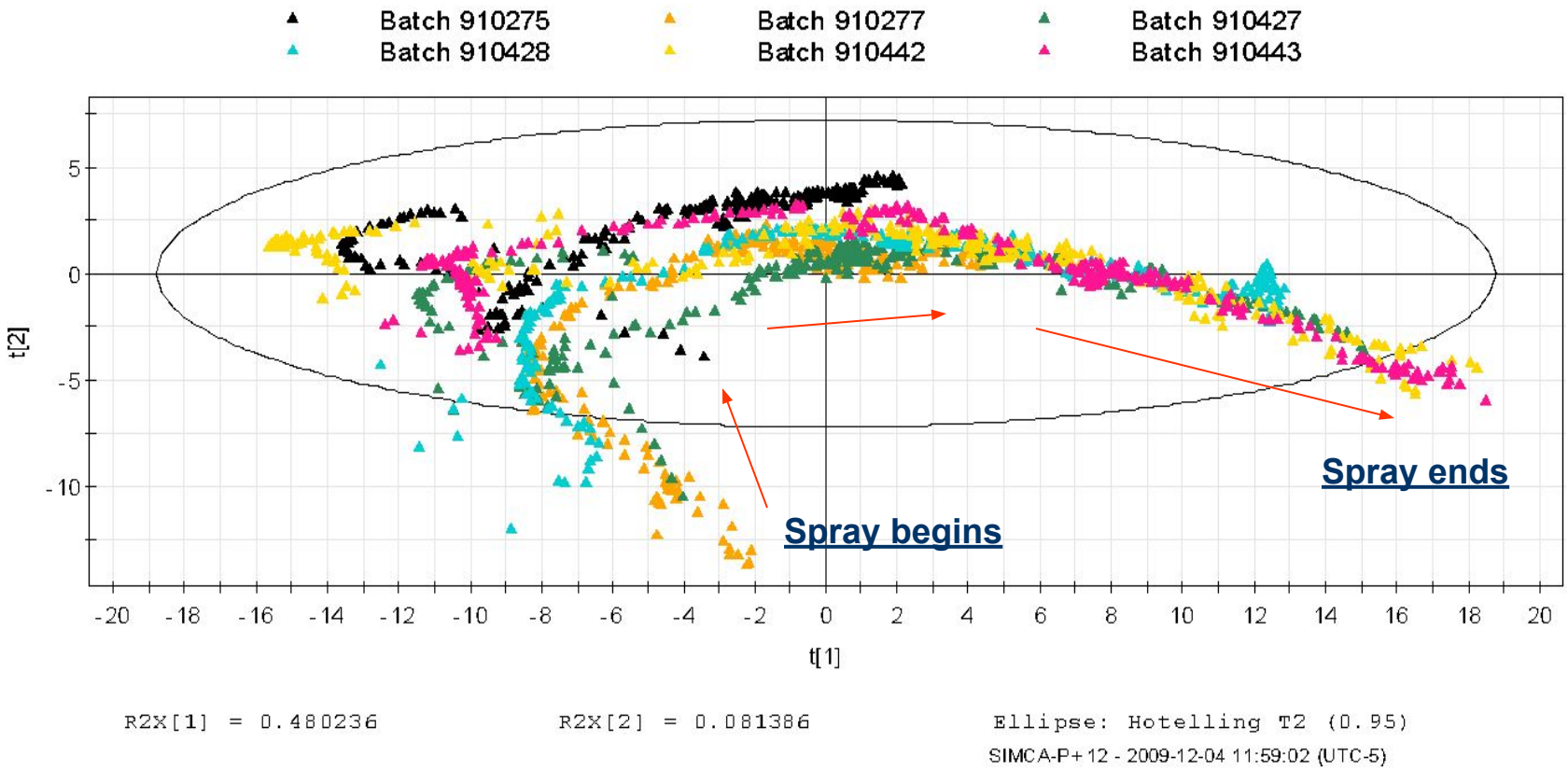
Batch/Multivariate Statistical Process Control (BSPC/MSPC)

Multivariate batch process trajectories



Variables included:

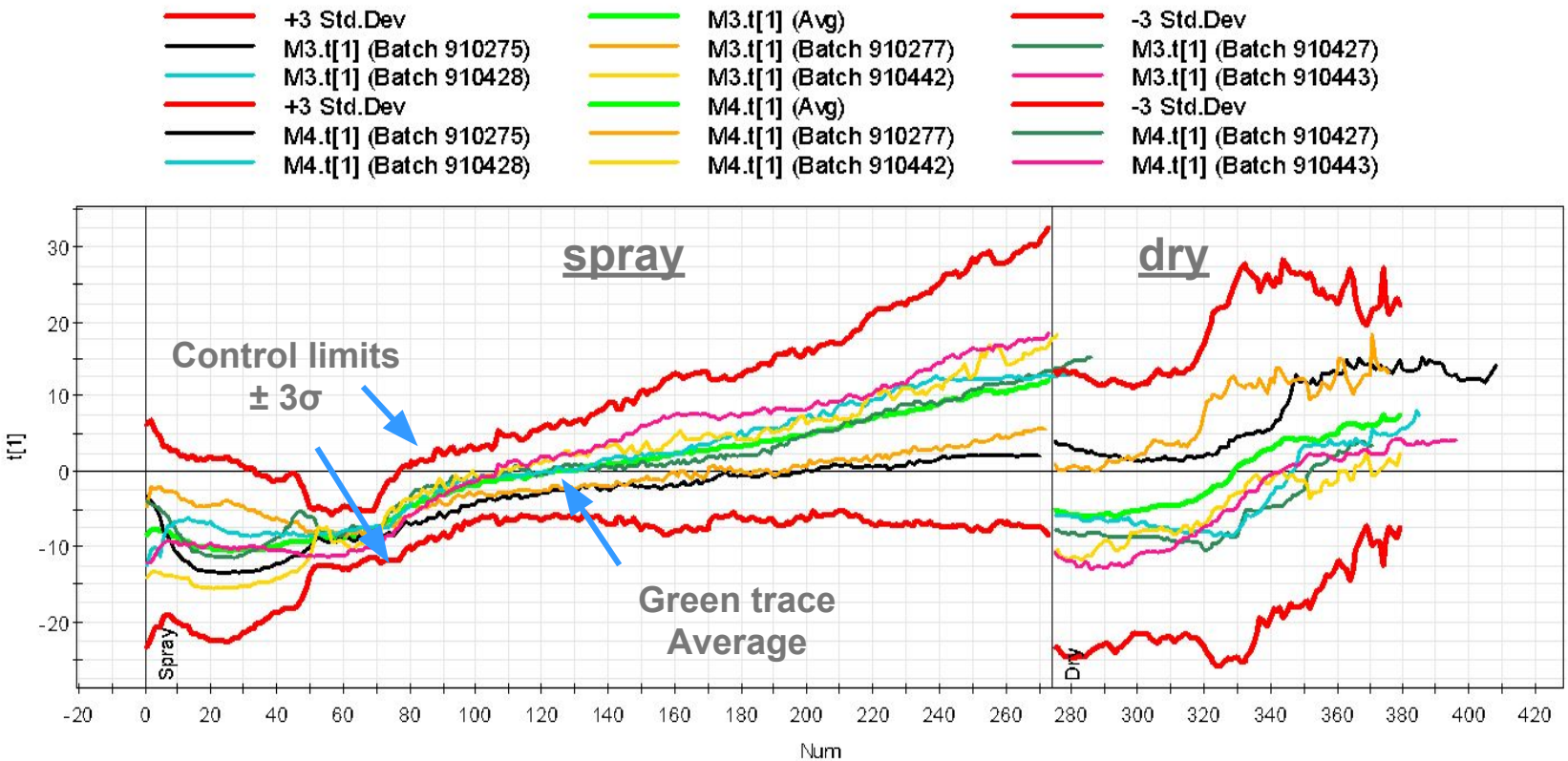
Chordlength data (number-based, volume-based), particle rate, particle velocity etc

Each point represents a combination of multiple variables at a particular time point

Batch Control Charting (Observation-level)

Batch Score Control Chart

Score Batch Plot (t1)

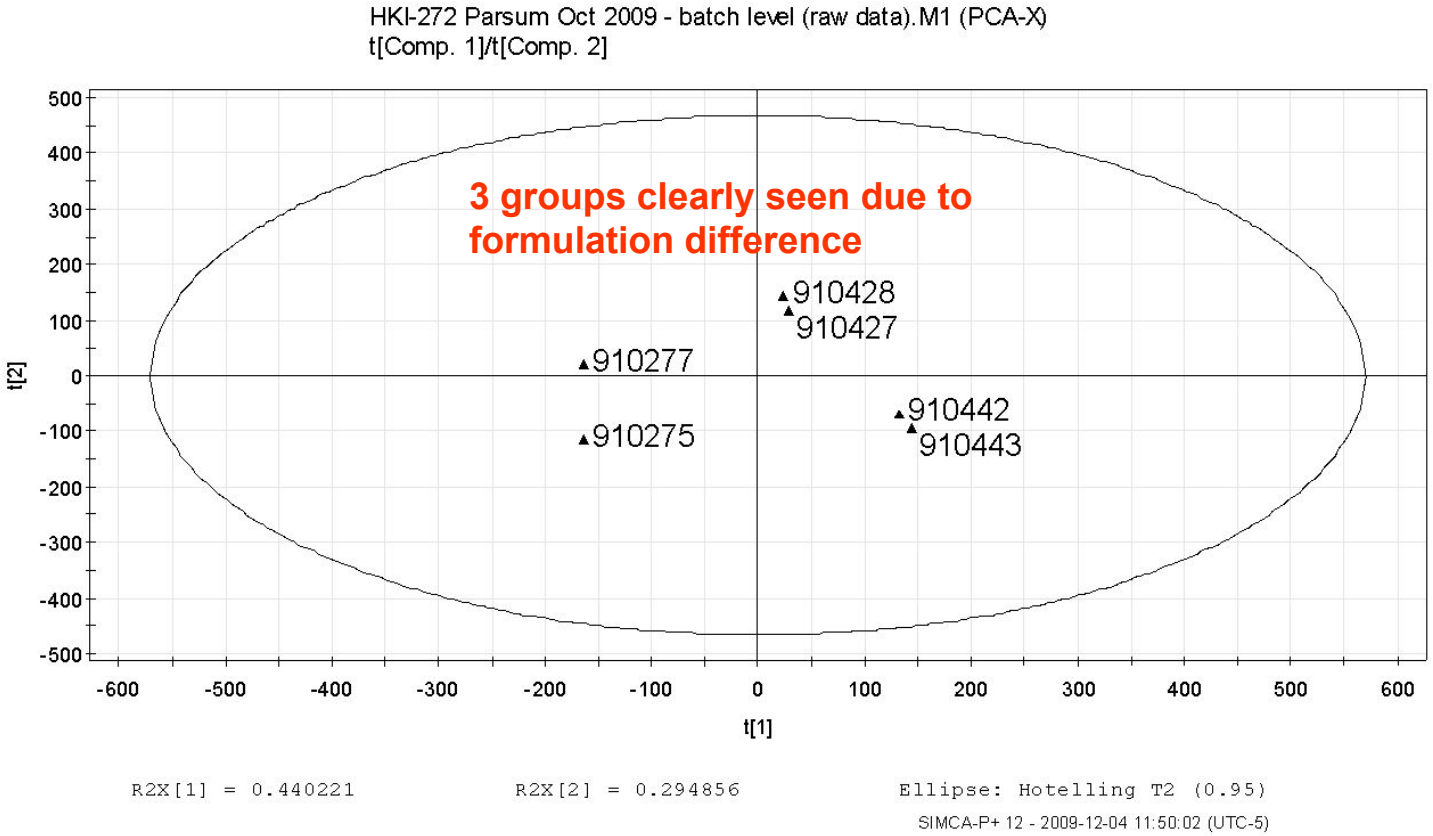


Variables included:

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