

In-line particle size analysis for high shear granulation processes

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Presentation Outline

- ▶ In-line particle size analysis
- ▶ PAT & QbD
- ▶ High shear granulation processes
- ▶ PARSUM's measurement principle
- ▶ Case studies
- ▶ Conclusion
- ▶ Q & A



In-line particle size analysis

- ▶ What is in-line?
- ▶ Why is it important?



Toxic

1. Particle size issues

- ▶ Particle size influences the behaviour of a particle in isolation and the way they interact to produce a collective effect.

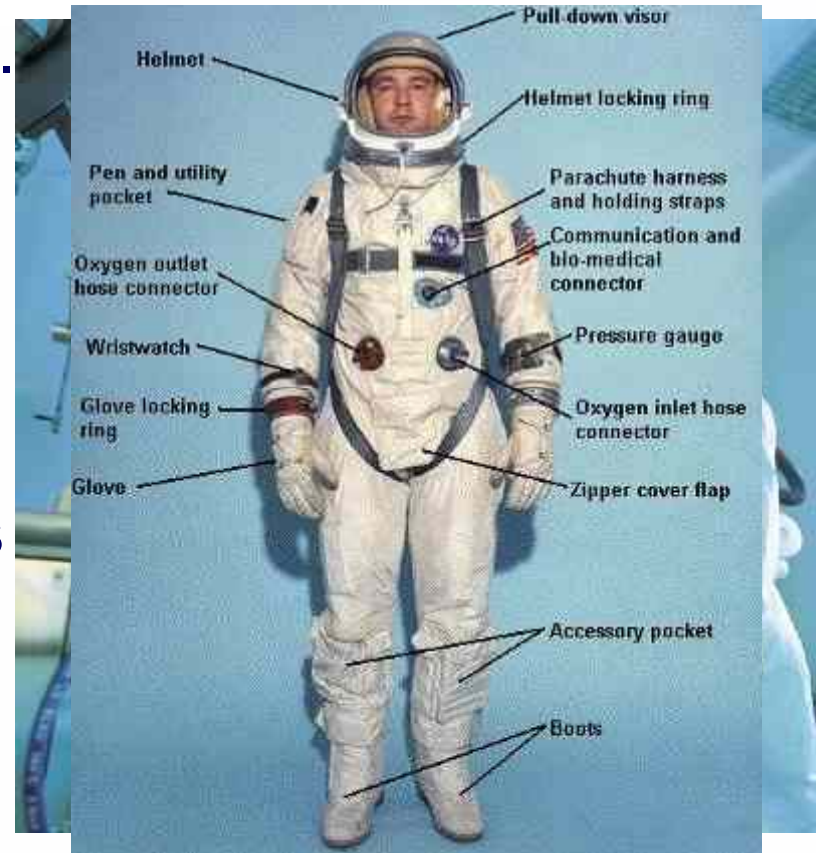


2. Industry Issues

- ▶ Minimize costs.
- ▶ Tighter control set points give a better product quality.
- ▶ Improve batch to batch consistency.
- ▶ For frequent start up or frequent product change, minimizes the time for the process to stabilize, increases in efficiency and throughput.
- ▶ For low throughput but high value product (e.g. pharma), better control minimizes wastage (higher yield).

3. Containment concerns

- ▶ Many drugs are highly toxic.
- ▶ Exposure must be limited.
- ▶ Operators must “suit-up” to take measurement samples typically restricted to 1 sample per batch.

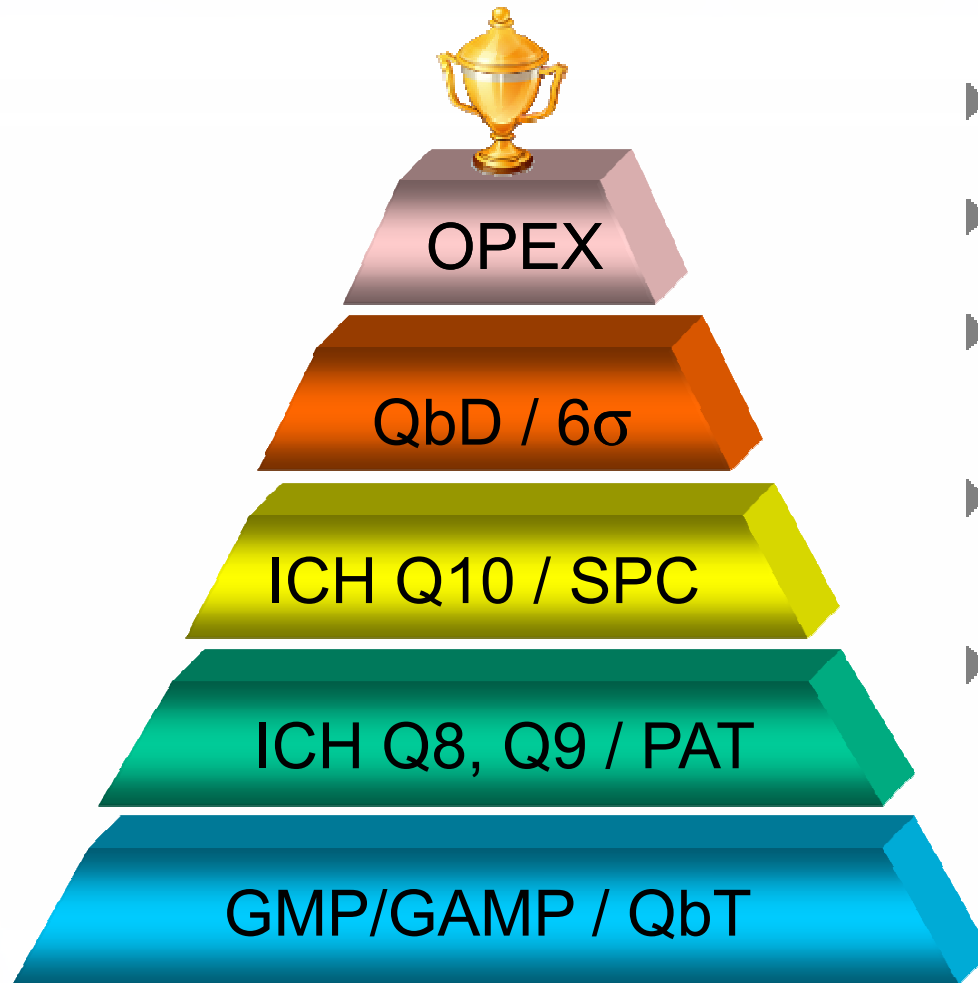


PAT & QbD

- ▶ PAT (Process Analytical Technology)
- ▶ QbD (Quality by Design)

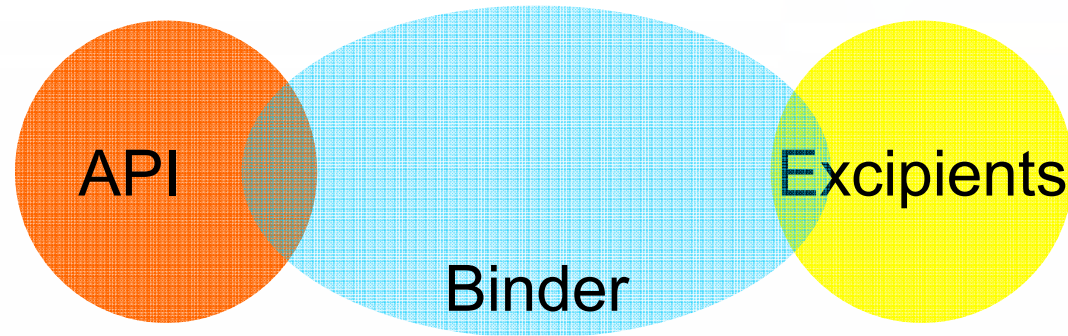


PAT enables QbD



- ▶ Define the Critical Control Parameters.
- ▶ Monitor and control endpoint and process.
- ▶ Enables continuous improvement and facilitates QbD approach.
- ▶ Generate mathematical relationships promoting process understanding.
- ▶ Real-Time process monitoring and control tools enable, ultimately, Real-Time Release.

High shear granulation processes



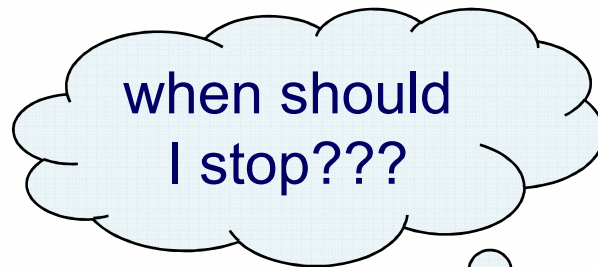
- ▶ Prevent segregation, improve flow, generate robust delivery system
- ▶ High shear wet granulation is a granulation process using high speed mixing blade.

High shear granulation processes

- ▶ Easy to over granulate.
- ▶ Over granulation may produce low porosity granules and affect the mechanical properties of the tablets.
- ▶ When to stop granulation? How to determine the end point?

High shear granulation processes

- ▶ End-point determination has been a problem.



High shear granulation processes

- ▶ End point control based on particle size was found to be the best.
- ▶ Some devices capable to follow median granule size growth but do not show in particle size distribution (PSD).
- ▶ Conversion to particle size distribution requires sophisticated mathematical software.



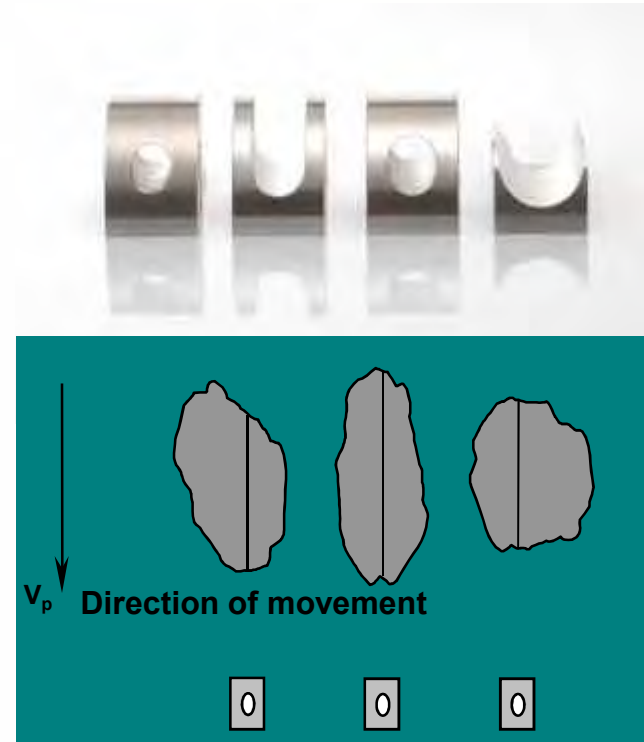
Acoustic Emission Spectroscopy (AES)

- ▶ 'Listen' to impacts of particles on impeller, vessel, particles and etc.
- ▶ Good for tracking some transition phases.
- ▶ Cannot be used as an indicator of phase completion.

High speed NIR

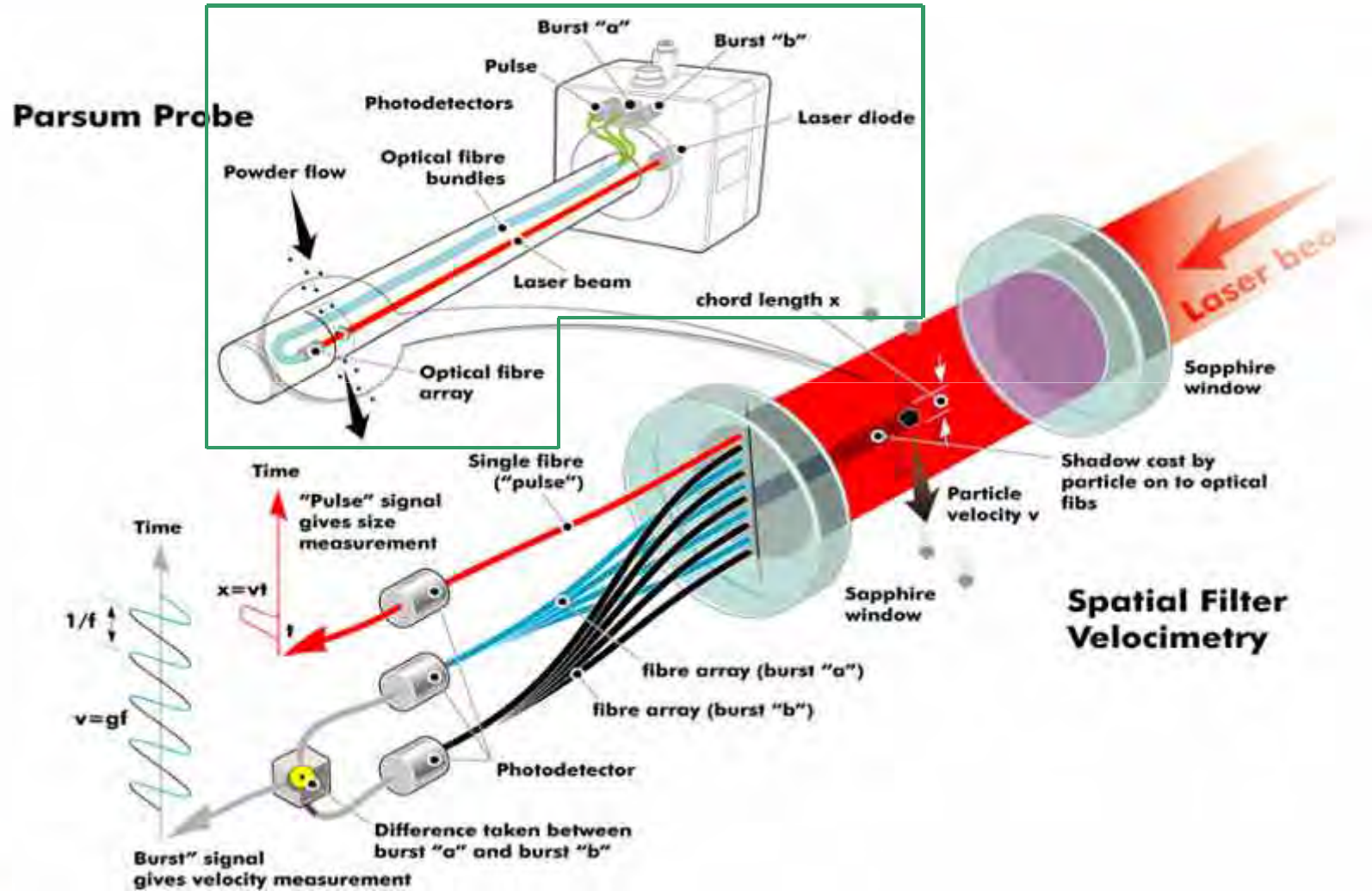
- ▶ Diode array based NIR
- ▶ Can predict the end of high shear mixing
- ▶ Good at tracking binder addition
- ▶ No detailed particle size information

PARSUM

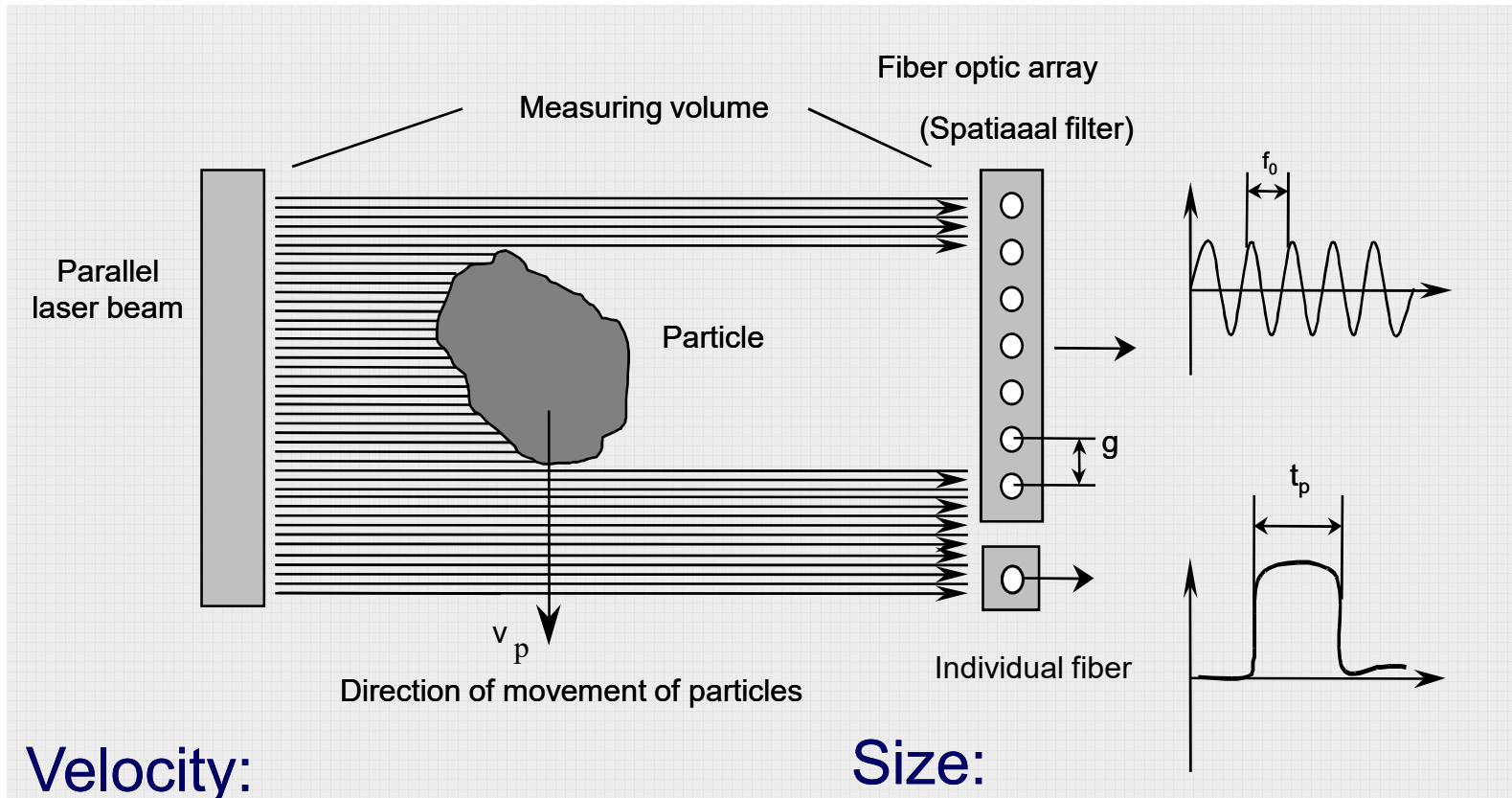


- ▶ Patented measurement technique.
- ▶ Chord length \equiv The link between two points on the perimeter of the measured particle projection face.

PARSUM



PARSUM



Velocity:

$$V_p = f_0 * g$$

$$[ms^{-1}] = [s^{-1}] * [m]$$

Size:

$$x_p = t_p * v_p - d$$

$$[m] = [s] * [ms^{-1}] - [m]$$

PARSUM

- ▶ Particle size : 50 μm – 6mm
- ▶ Particle velocity : 0.01m/s – 50m/s
- ▶ Pressure : < 4 bar
- ▶ Temperature : -20°C – 100°C

- ▶ Air purge keep the sapphire windows clean.
- ▶ No moving part.
- ▶ Disperser unit allows high concentration measurement.
- ▶ No recalibration required.



Case Study 1

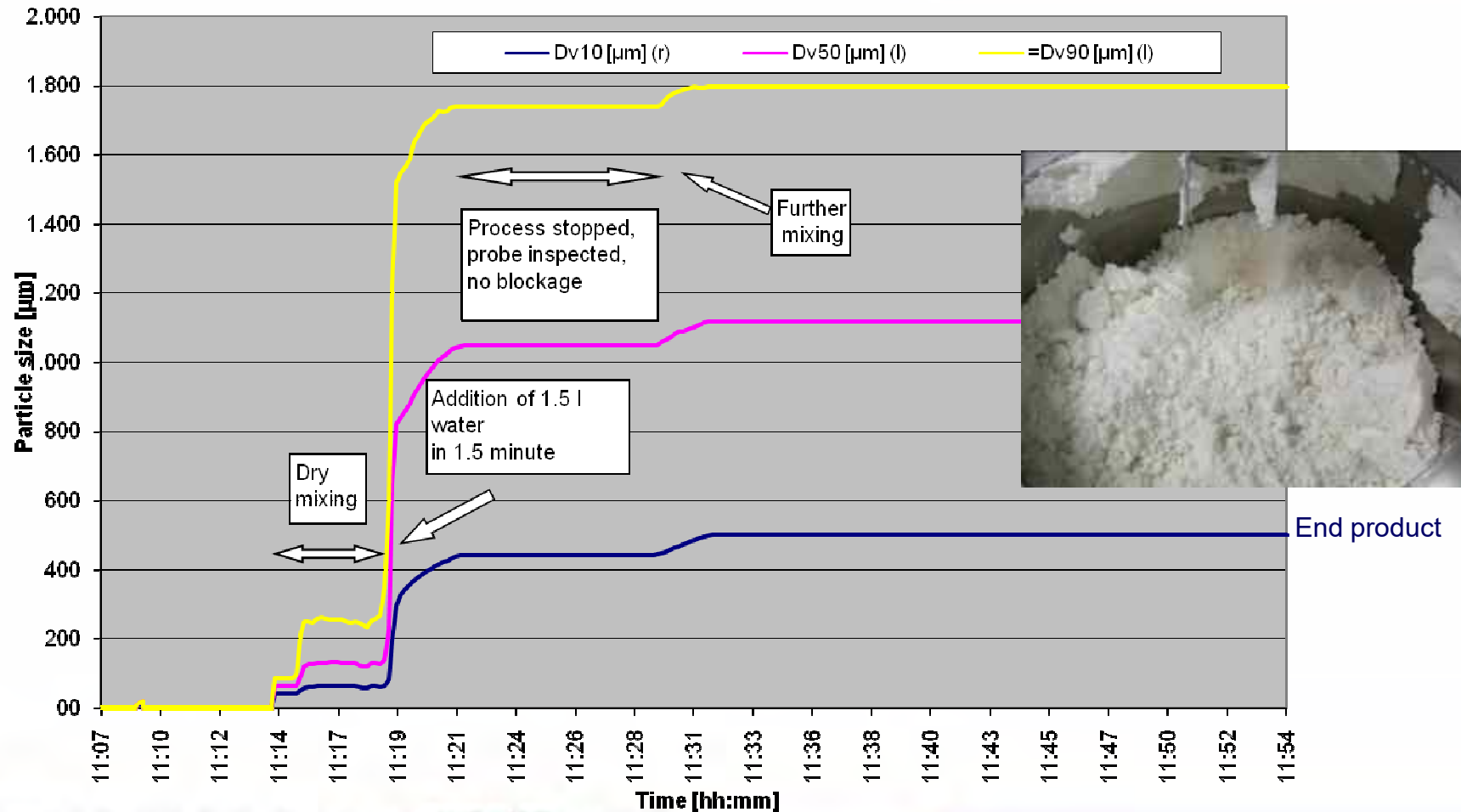
- ▶ Diosna Dierks & Söhne GmbH (Osnabrück)
- ▶ Goal: To demo the suitability of IPP-70 in smaller mixers.



Pilot Processor System P/VAC 10 - 60

Case Study 1

Test Parsum Inline Particle Probe IPP 70-S
 Dlosna Dierks & Söhne GmbH, Osnabrück,
 Test 2 Mixer P VAC 1-60 (VAC50)



Case Study 2

- ▶ Goal: To demo suitability of IPP 70-SL in larger mixers.



IPP 70-SL (60 cm)

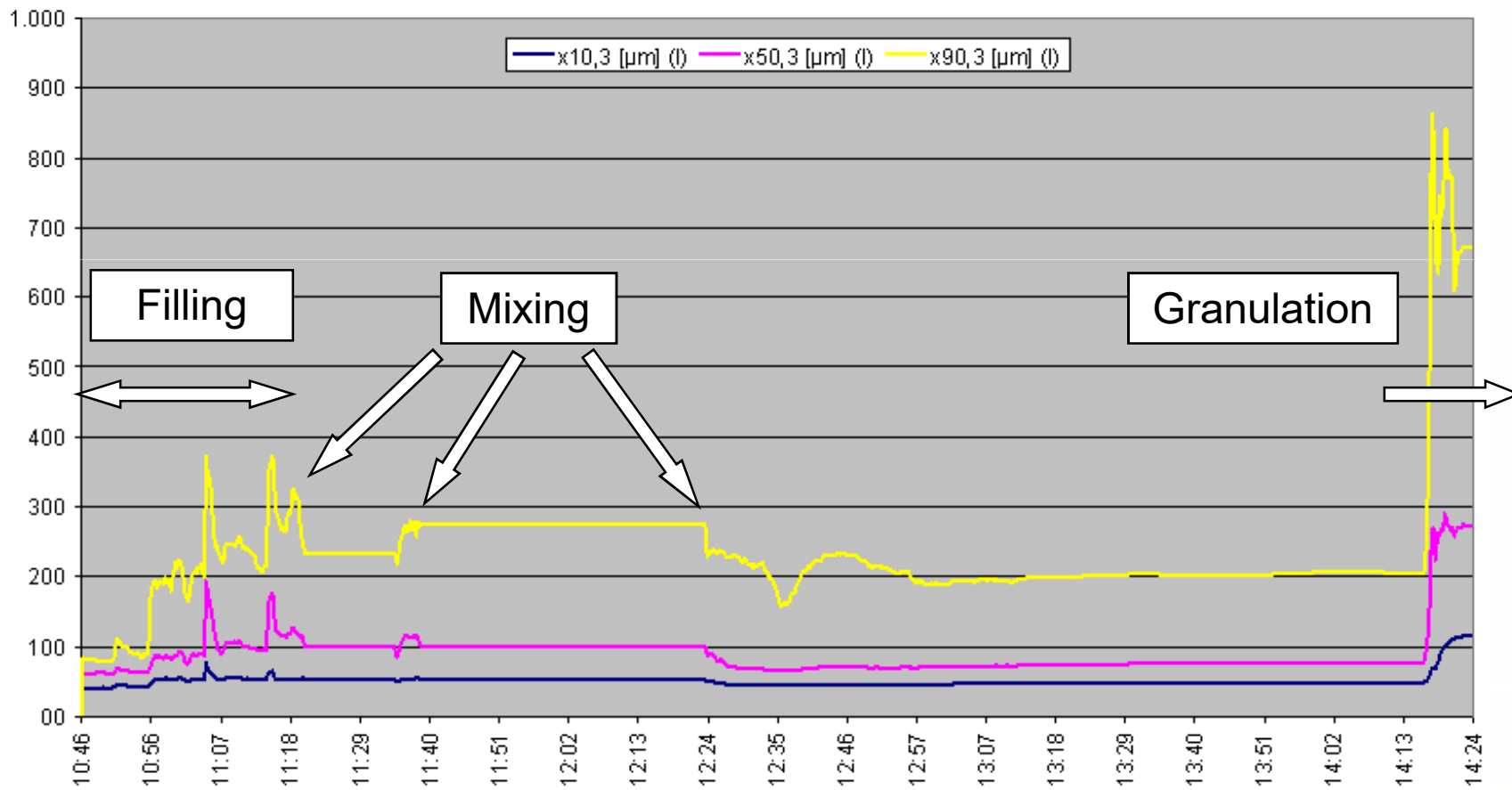


Case Study 2



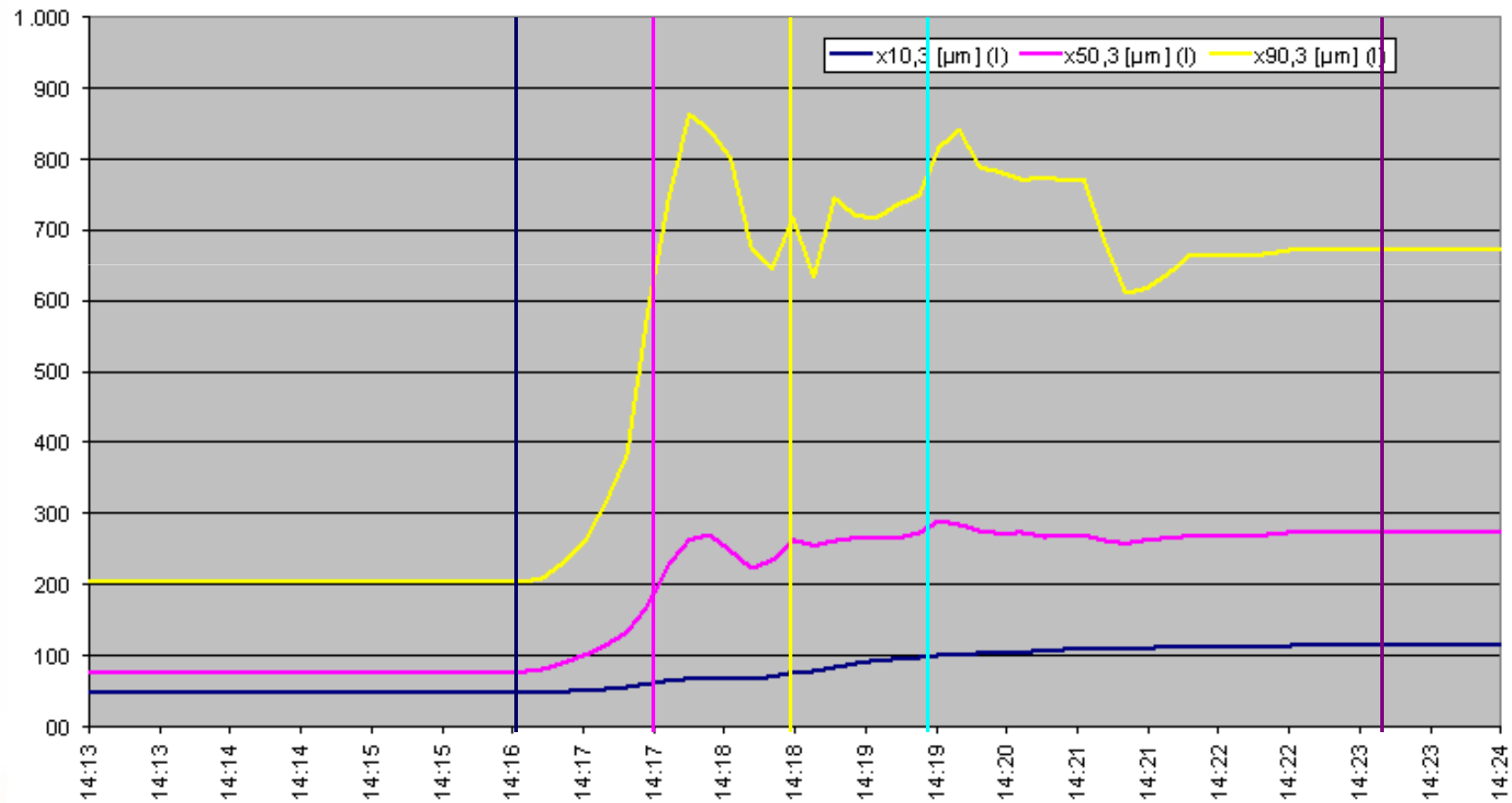
Case Study 2

Test Parsum IPP70-SL



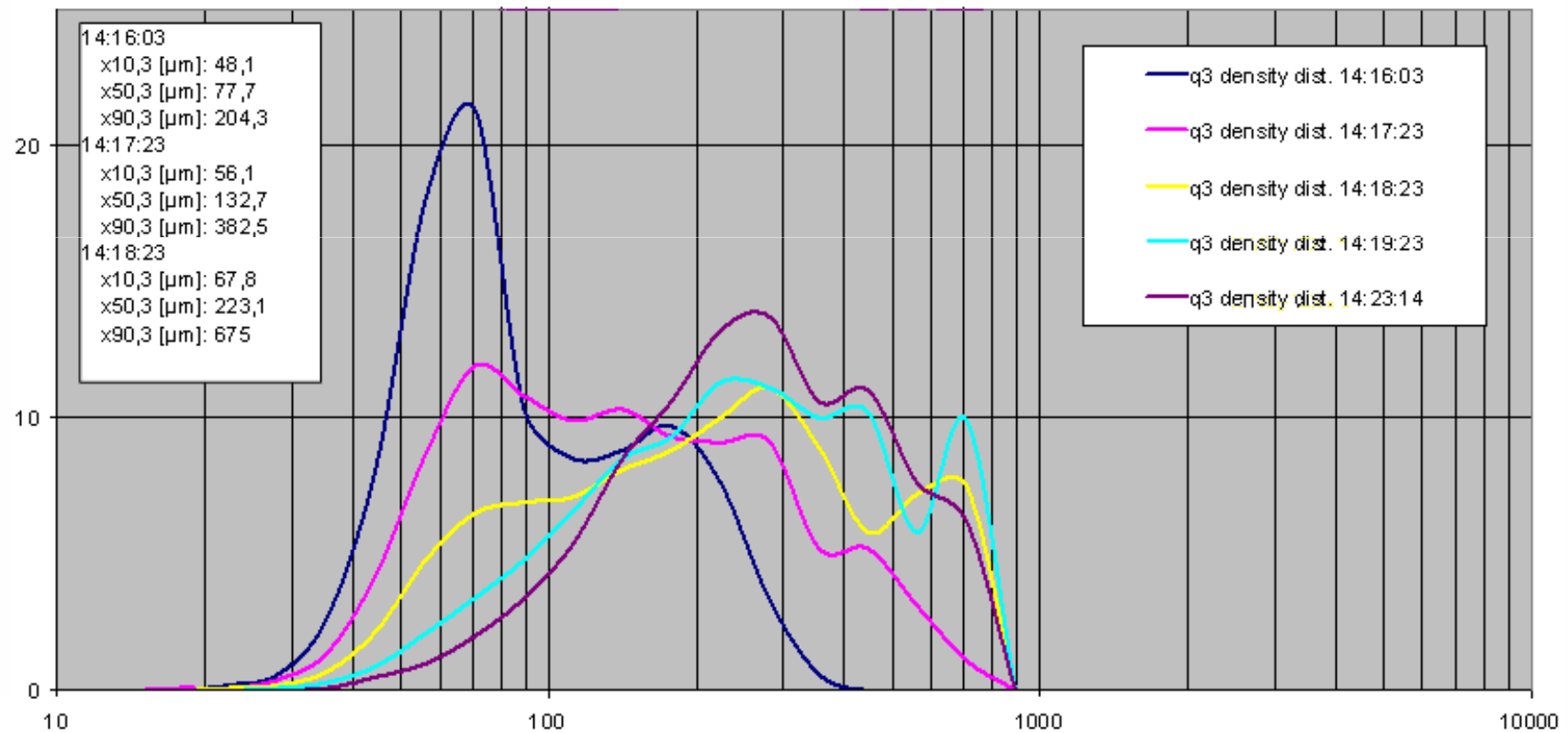
Case Study 2

Granulation phase



Case Study 2

Granulation phase



Case Study 3



Goals: Monitor a batch granulation process, gain in depth understanding, detect the process phases and endpoint

Product: 40kg/batch mineral product, $Dv50 = 50\mu\text{m}$

Equipment: R05 / T (From Eirich)

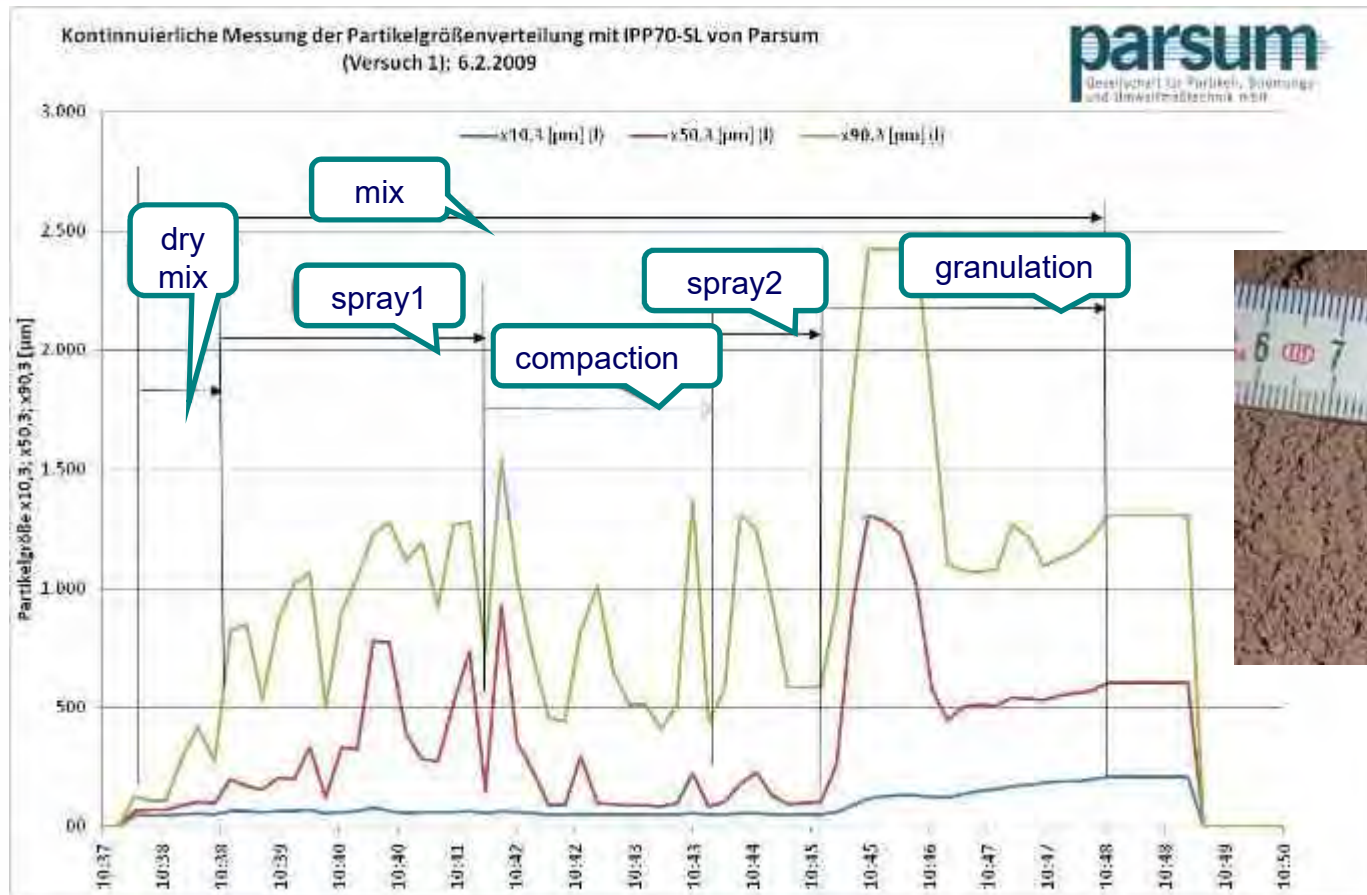
Installation: IPP70-SL, Disperser D23



Measurement zone of D23



Case Study 3



End product

Conclusion

- ▶ In-line particle size analysis
- ▶ PAT & QbD
- ▶ High shear granulation processes
- ▶ PARSUM's measurement principle
- ▶ Case studies



THE END

Any Question?

