Near Infrared Spectroscopy for flowing powder API monitoring – a PAT application for « Quality by Design »

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Abstract

- **Context/Rationale**: Bulk powder flow is a frequent operation in pharmaceutical processes. Such flows occur at the entrance of a compression unit and its characteristics are of great interest in order to maintain blend uniformity.
- **Objectives**: This work is aimed at developing a PAT application based on the use of the NIR Technique for in-line flow characterization of a solid oral dosage pharmaceutical formulation.
- **Methodology**: A bench scale hopper system was assembled to replicate process environment. An NIR process spectrometer and probe were chosen to collect in-line spectral data of the powder flow of an ibuprofen based formulation. The non-contact sampling interface allowed the collection of representative process powder flow spectra without interfering with the flow attributes. A PLS chemometric model was developed using laboratory prepared samples to allow quantitative determination of the flowing powder`s active concentration.
- **Results**: Static sample spectra had a high degree of reproducibility. The model's standard error of prediction was 2.93 % API with a R^2 of 0,991. Flowing blend powder spectra and API estimates showed some variation during runs. This is consistent with the variations seen in the model samples and was expected. Furthermore, flow speed did not affect spectral variation in the studied range.
- **Conclusion** : The average values for flowing blend were close to the theoretical API concentration indicating that the average measurement is correct. The developed model is considered very promising and some improvement would lead to its final acceptance at production scale as a PAT tool.

Objectives

- Establish if NIR spectroscopy is a valid method for cohesive multicomponent non-aerated powder flow characterization
- Estimate the influence of flow rate on blend homogeneity or segregation through NIR real-time testing

Materials and Methods

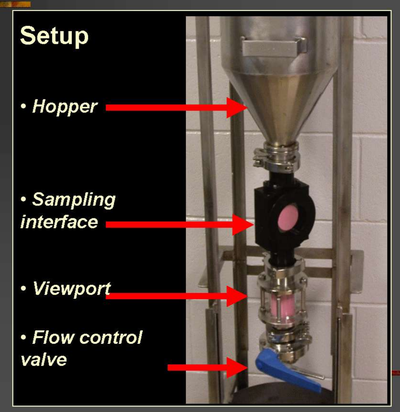
Part 1

- Building a predictive model
  - Partial Least Squares (PLS)
  - Blend samples of different API %

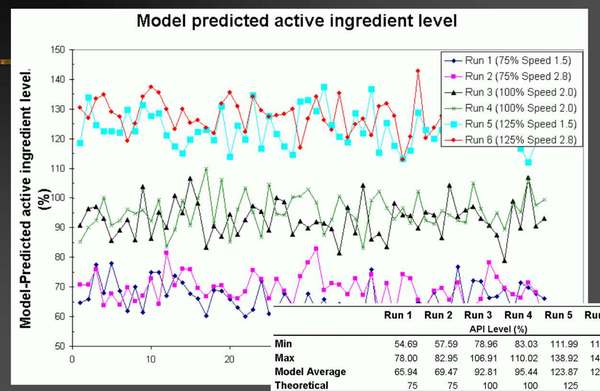
Part 2

- Applying the model
- Design of experiments
  - Flowing blends of different API %
  - Different flow rates

Setup



Results and Conclusions



	Run 1	Run 2	Run 3	Run 4	Run 5	Run 6
	API Level (%)					
Min	54.69	57.59	78.96	83.03	111.99	112.92
Max	78.00	82.95	106.91	110.02	138.92	142.84
Model Average	65.94	69.47	92.81	95.44	123.87	127.62
Theoretical	75	75	100	100	125	125
Std Deviation	5.51	5.01	5.99	5.81	6.62	5.79
Flow Rate (kg/min)	1.5	2.8	2.0	2.0	1.5	2.8

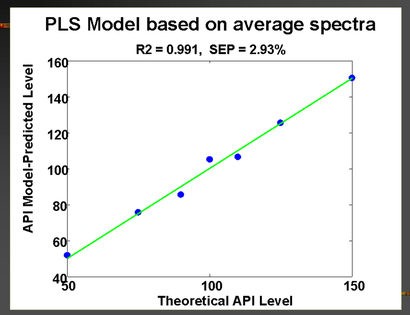
Introduction

- According to the FDA PAT Draft Guidance, the desired state of pharmaceutical manufacturing and regulation may be characterized by the following criteria:
  - Continuous real time quality assurance;
  - Product and process specifications based on a mechanistic understanding of how formulation and process factors affect product performance;
  - Product quality and performance are ensured through the design of effective and efficient manufacturing processes
- Cohesive powders are used in more than 70% of Pharmaceutical processes.
- There are no efficient models for cohesive dense powder flow behaviour prediction
- There is a need for in-line analyzers to allow process improvement and real time quality control

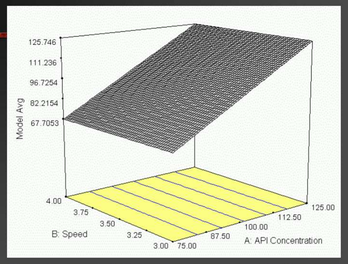
Design of Experiments (DOE)

Run (#)	Active Ingredient Level (%)	Powder Flow Rate (kg/min)
1	75	≈ 1.5
2	75	≈ 2.8
3	100	≈ 2.0
4	100	≈ 2.0
5	125	≈ 1.5
6	125	≈ 2.8

Results and Conclusions



Results and Conclusions



- Flowing blend API was successfully predicted by NIR method for different concentrations
- Flow rate does not affect blend homogeneity or method`s validity