Top Spray Granulation PAT monitoring by NIR: calibration vs. PCA trend approach

Andrea Gelain[1], Giuseppe Buratti[1], Emiliano Genorini[2], Gabriele Inverni[1]
Freund-Vector European Lab[1], Villasanta (MB); Viavi Solutions Italia[2], Vimercate (MB)

PURPOSE

To determine the endpoint for Top Spray Granulation using NIR technology. To establish the correlation between the Moisture Content (expressed as Loss on Drying), the Particle Size Distribution (PSD) of the mixture and the response of the NIR device. To find a mathematical and statistical approach to the in-process control using derivative method, PCA calculation and trend approach.

METHODS

A placebo formulation (shown in table 1) was granulated in this study. The process was performed using fluid bed (Freund-Vector VFC Lab3) equipped with Viavi MicroNIR PAT-U device. The device is connected to the fluid bed with a welded flange. The mixture was granulated with top spray technology and later dried.
Two runs were performed. The load of dry blend was adjusted for each type of equipment to achieve appropriate product movement. The process was replicated with the same formulation and process conditions to demonstrate the robustness of this method. LOD was determined at regular intervals using a thermobalance (Mettler Toledo MJ33). PSD was also determined using a graphical imaging device (Sympatec QicPic). Datas were analyzed and processed by Unscrambler software.

Table 1 - Formulation - Blend		
Component	*Quantity (g)*	*%*
Lactose 200 mesh	1000	50
Pregel. Starch	700	35
MCC	300	15
Total	*2000*	*100*
Formulation - Binding solution		
PVP K30	100	10
DI Water	900	90
Total	*1000*	*100*

RESULTS

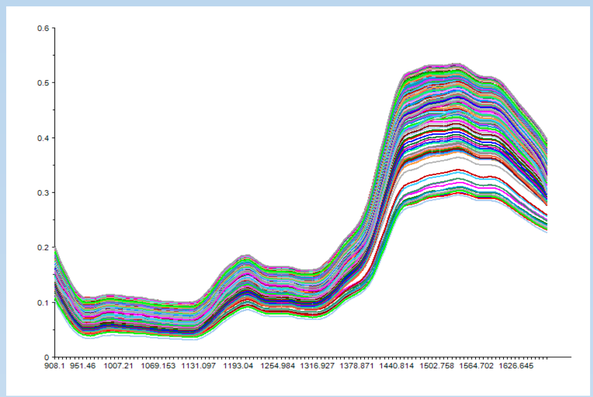

Figure 1

Table 2 - Process Parameters			
Inlet air Temp. (°C)	50 - 60	Process time (min)	90
Product Temp. (°C)	27 - 28	Spray Rate (g/min)	25 - 30
Airflow (m^3/hr)	80 - 110	LOD (%)	3 - 10

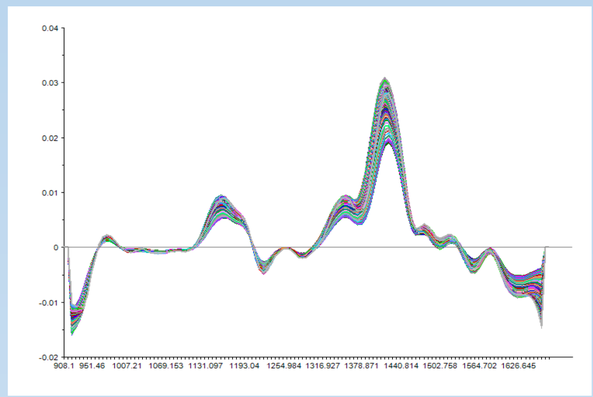

Figure 2

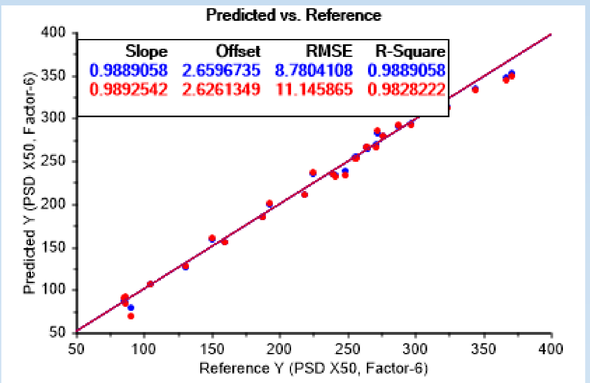

Figure 3

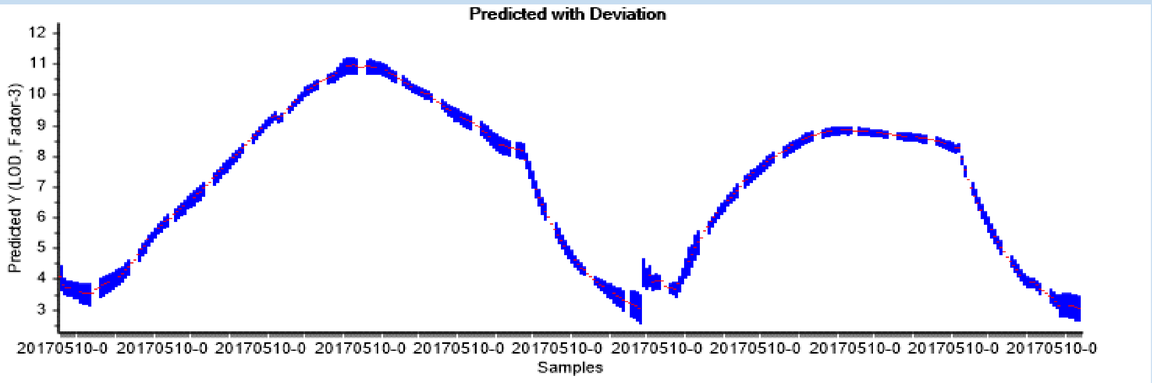

Figure 4

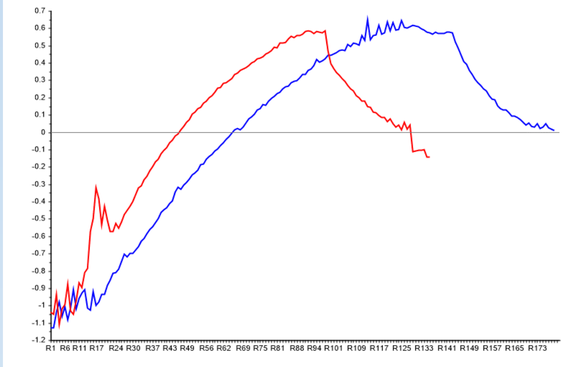

Figure 5

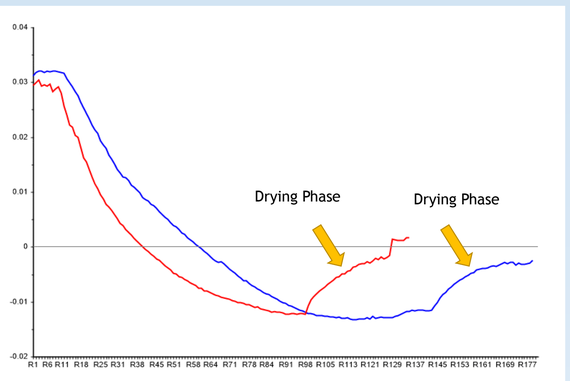

Figure 6

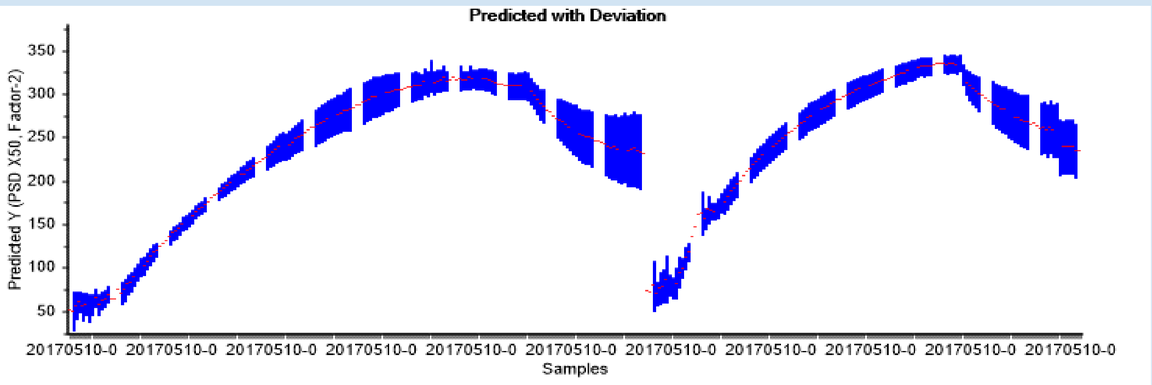

Figure 7

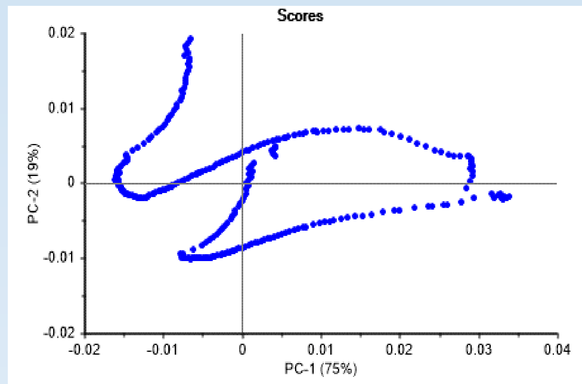

Figure 8

Freund-Vector VFC LAB 3

The Absorbance curve and the 1st derivative are shown in Figures 1-2. The correlation between the measured PSD and the absorbance values is shown in fig. 3. The high R^2 shows that there is a strong correlation between the real datas and the response of the NIR, confirming that the model is robust. In fig 4 are shown the calculated values of LOD and SD of the two batches based on the calibration curve made for batch 1.The Principal component analysis confrontation between the two replicas is shown in fig. 5.In fig.6 is shown the 1st derivative PCA trend of the process. The calculated PSD of the two batches based on the calibration curve of batch 1 is visible in figure 7. In fig. 8 is visible the similar trend of the two processes in terms of PCA.

Viavi MicroNIR PAT U Equipment

CONCLUSIONS

This process shows a very strong correlation between the absorbances read by the NIR instrument and the determined LOD and particle size distribution. It is clearly visible the similar trend of the process repetitions. This indicates that the model is reproducible. When the process shows no more changes, the principal component analisys graph tends to a plateau, so it is possible to locate the endpoint of the granulation process in terms of moisture content and particle size growth. At the end of the granulation it is possible to locate a trend change that represents the drying phase. A future developement of this study can lead to a real time control of the process in terms of the product carachteristics instead of the process parameters, with the aim of an integration with the automatic control system.