# PAT Monitoring of Coating Pan by NIR: PLS Method Calibration Approach

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## PURPOSE

To follow the coating pan process by means of NIR technology and to determine the weight gain and the coating thickness of the coated tablets in real time. To establish the correlation between the physical properties of the tablets and the response of the NIR device. To demonstrate the independency from the coating material used to achieve a correct process monitoring. To find a mathematical and statistical approach to the in-process control using derivative method, PLS calibration and cross-validation method.

## METHODS

Placebo tablets (round, convex, 8mm diameter, 4mm thickness, 250 mg) were used as coating cores in this study. The set of processes were performed in coating pan (Freund-Vector LDCS Pilot) set up with 8L pan, Schlick spray gun and Viavi MicroNIR PAT U device. The device was positioned in the coating pan through the front door, attached to the spray bar parallel to the spray gun. A clearance of about 3 cm was set between the NIR device and the pan baffles.
The load of dry cores was adjusted for the type of equipment to achieve appropriate product movement and the correct quantity was determined to be 4000 g. The process was replicated using two different coating agents (HPMC and PVA based ready-to-use coating systems) to demonstrate the independency from the material used. The data were analyzed and processed using Unscrambler software.

*Table 1 - Coating Suspensions*

| Component | Quantity (g) | % |
|---|---|---|
| Opadry I white | 400 | 12 |
| Opadry II blue | 400 | 12 |

## RESULTS

The 1ST derivative of the absorbance curve is shown in Figure 1. 30 tablets were sampled every 15 minutes during the process, the weight gain was measured using a two-decimal scale every 15 minutes and the coating thickness was measured every 30 minutes by a three-decimal micrometer. 3 batches per coating materials were used together to build a calibration curve, the measured samples were correlated with the NIR response by the PLS method. The high $R^2$ shown in Figure 2 shows that there is a strong correlation between the real values and the response of the NIR, confirming that the model is robust.

A 4th batch was run for every coating agent as an «unknown» batch to verify the model. The batch was sampled and measured in the same way, and the values were compared to the thickness and weight values calculated by the software using the calibration curve. Fig. 4 and 6 represent the comparison between the measured coating thickness and the calculated one. Fig. 5 and 7 represent the weight gain comparison. Fig. 3 represents the in-line weight gain prediction calculated by a software with relative standard deviation.

*Table 2 - Process Parameters*

| | | | |
|---|---|---|---|
| Inlet Air Temp. (°C) | 65-80 | Process Time (min) | 150 |
| Product Temp. (°C) | Approx 45 | Spray Rate (g/min) | Approx 25 |
| Airflow ($m^3$/hr) | 130 | Pan Speed (RPM) | 20 |

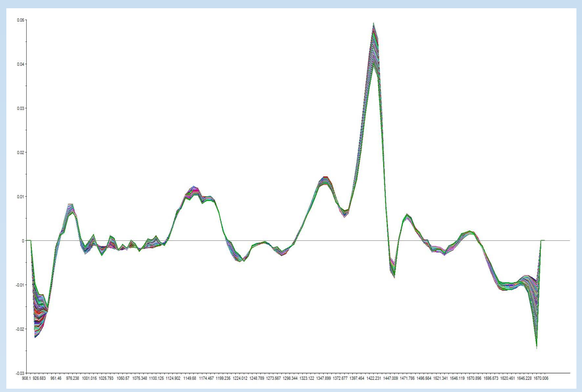

Figure 1

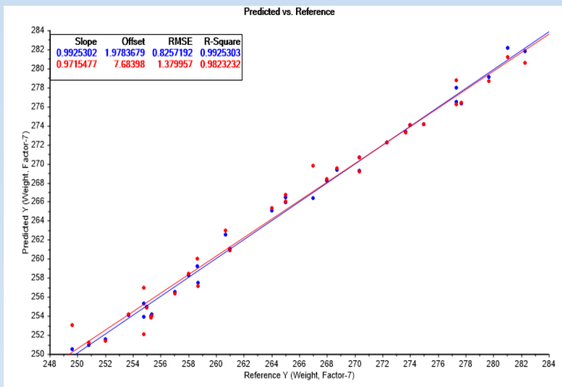


Figure 2

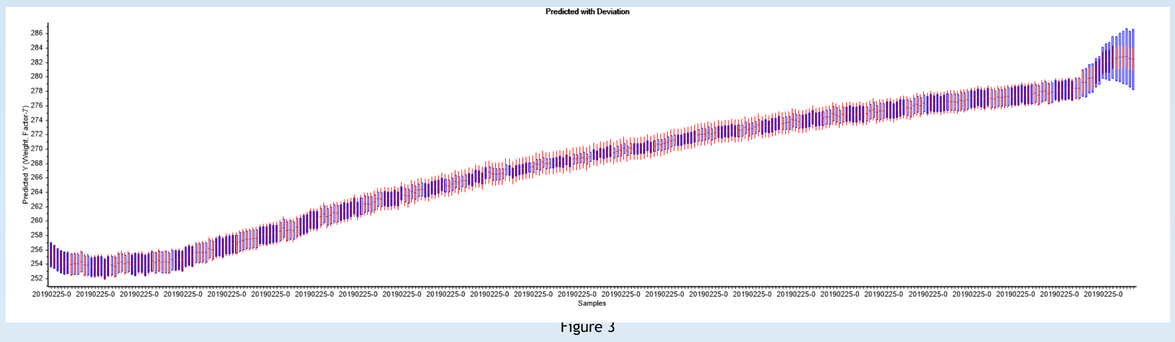


Figure 3

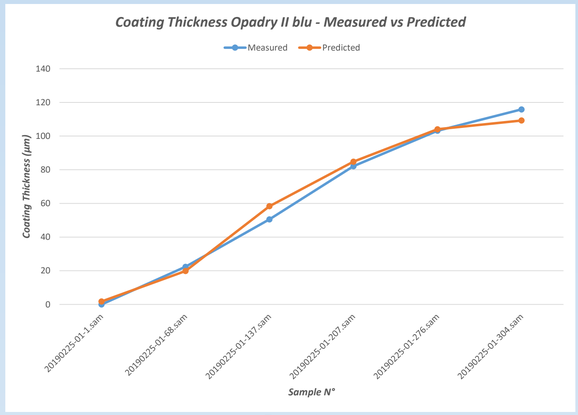


Figure 4

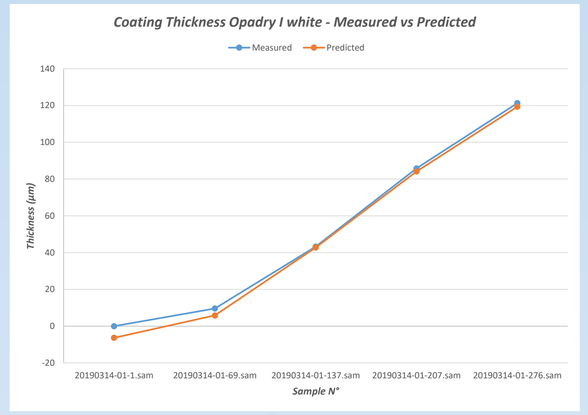


Figure 6

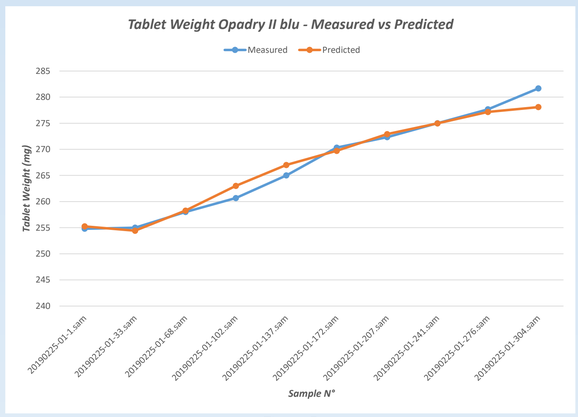


Figure 5

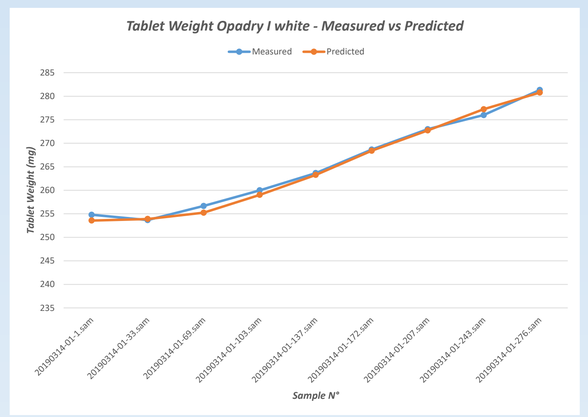


Figure 7

Viavi MicroNIR PAT-U Equipment

LDCS Pilot coating pan

## CONCLUSIONS

The process shows a very strong correlation between the absorbances read by the NIR instrument and the determined coating thickness and weight gain. This indicates that the model is reproducible. The reproducibility and the precision of the PAT monitoring can allow process control without the need for constant sampling and at-line analysis. This allows precise in-process control over the product and provides the possibility to spare process time, energy and raw materials. Future development of this study can lead to an integration of the PAT technology with the control software of the coating pan and a real time control of the process in terms of product characteristics instead of the process parameters, with the aim of integration with the automatic control system. This integration can also be developed to design a continuous manufacturing process that must be kept constantly under control to guarantee the reproducibility of the final product.