SPECTRAL ENGINES

APPLICATION NOTE

SMART INDUSTRY

Next generation quality control in future pharmaceutical processes

New pharmaceutical manufacturing processes require next-generation quality monitoring tools

Near-infrared (NIR) spectroscopy enables the determination of the amount of active pharmaceutical ingredients (API) and excipients in pharmaceutical production. The quality of pharmaceutical ingredients is absolutely critical in ensuring patient safety. Global pharmaceutical revenues increased to over one trillion US dollars in 2014. A capacity to measure quality-related costs has been advocated as an important component of quality improvement with quality related costs ranging from 10–30 per cent of sales and 25–40 per cent of operating expenses.[1]

Pharmaceutical production is traditionally carried out in batch processes. The process phases of pharmaceutical production include steps like granulation, blending, tableting, and coating. The quality of raw materials and end-products needs to be checked but also the quality of each of these manufacturing steps.

Nowadays more and more continuous manufacturing concepts are also studied in the pharmaceutical industry. Real-time quality measurements will play an even more important role when continuous manufacturing is used in the future. Quality control should offer operators real-time information on production quality to ensure the quality attributes of the final product. One of the latest trends in the pharmaceutical industry is to aim towards personalized medicines which will mean that pharmaceutical products will be produced in small batches utilizing novel printing technologies.

This fragmented manufacturing concept will challenge pharmaceutical product inspection systems, since quality control should be done for all products, not just small samples from big batches. Both continuous manufacturing and printable medicines are completely new manufacturing concepts in the pharmaceutical sector, and they present more challenges for measurement and inspection systems, which need to deliver reliable and real-time quality information about production.

Spectral Engines' sensors offer real-time data on pharmaceutical processes

Spectral Engines has developed miniaturized near-infrared NIRONE™ Sensors that can be used in several pharmaceutical process quality measurements. Near-infrared spectroscopy has several benefits, such as fast analysis (less than a second), minimum sample preparation (process measurement possible), and good accuracy (better than 0.5% for most of ingredients).

Thanks to their small size and high signal-to-noise ratio, Spectral Engines' sensors are easy to integrate into traditional batch processes, continuous manufacturing lines and even into modern inkjet printers.

Benefits of Spectral Engines' sensors:

- Real-time measurement data realized with compact spectral sensors
- Process information captured and process failures detected
- End-point analysis in mixing or drying processes
- Trends of continuous manufacturing create more information to detect quality problems in production

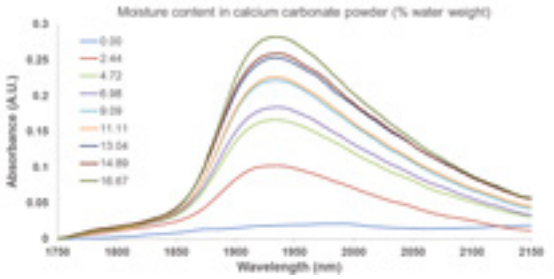
Spectral Engines sensors can be used as stand-alone reflection sensors or they can be combined with off-the-shelf fiber optical probes. The sensors can be easily deployed and can be used as stand-alone reflection sensors or they can be combined with off-the-shelf fiber optic probes. Their cost-effective price make it possible to use them in several locations ffor example in a continuous pharmaceutical production line. Spectral Engines' sensors are available with a specification of 1350–2150 nm and they offer higher sensitivity than a typical linear-based analyzer.

1 Muhammad Jawad Bhatti et al., J Dev Drugs 2014, 3:3; Cost of poor quality in a pharmaceutical industry: A case study, GMP, GCP & Quality Control, September 25-26, 2014 Valencia Convention Centre, Spain

Ultra-low moisture analysis of pharmaceutical tablets

The University of Leeds has examined the feasibility of Spectral Engines' sensors to detect moisture content. The moisture content of calcium carbonate powder was determined using the Spectral Engines NIRONE™ Sensor 2.2 with integrated light source operating at 50% of the light intensity, using an immersion NIR reflectance probe (50 scans averaged, 0.2 ms integration time, 1 nm resolution). The water–calcium carbonate mixtures were prepared in-situ using a fluidized bed. The moisture varies from 0 - 16.67%. Moisture concentration was tested successfully while extremely good stability was observed.

Moisture information is required in many process steps, such as those required by GlaxoSmithKline (GSK) for their process tableting pilot line. GSK is one of the world's largest pharmaceutical and health care companies and is also an industrial partner in the ProPAT consortium which is a 4-year EU-funded research program related to novel sensors and IoT solutions.



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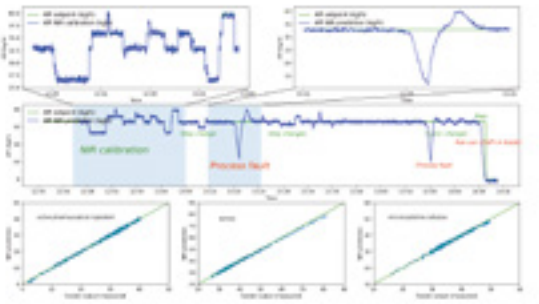
Real-time quality sensors for continuous manufacturing process

Spectral Engines' Near-infrared sensors were installed into a continuous pharmaceutical process line. Three main components – Active Pharmaceutical Ingredient (API), Lactose, and Micro-Crystalline Cellulose (MCC) – were monitored in real time. The calibration model was carried out over 15 minutes by changing the concentrations in a controlled manner. Process failures in the feeders were detected during the manufacturing processes. Spectral Engines' sensors offered reliable real-time information from continuous manufacturing and this information was used to help operators identify malfunctions in the process. The data was very reliable and accurate for all components.



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Concentration measurement of printable pharmaceutical products

Spectral sensors can also be used in the quality control of pharmaceutical products when products are manufactured using novel ink-jet printing technologies. Åbo Akademi University in Finland has evaluated Spectral Engines' portable sensors in the quality control of printable orodispersible formulations. Four different orodispersible dosage forms containing two poorly soluble drugs (levothyroxine and prednisolone) were produced on two different edible substrates by means of piezoelectric inkjet printing. In addition, the stability of drug inks over the course of 24h as well as the mechanical properties and disintegration behavior of the printed units were examined. It was verified that the models were capable of clustering and predicting the drug dose in the formulations, with both Q2 and R2Y values from 0.94–0.99.

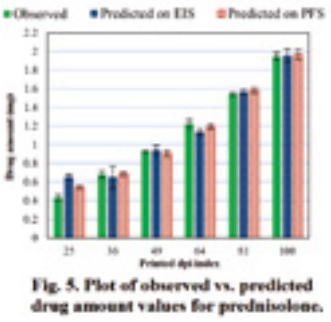

Fig. 5. Plot of observed vs. predicted drug amount values for prednisolone.

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Conclusion

Spectral Engines' compact and cost-effective spectral sensors enable fast, reliable and non-destructive way to measure quality attributes of pharmaceutical processes. Spectral sensors can be used as portable sensors in raw material inspection or quality checks of final products. Sensors can also be integrated in batch processes or continuous pharmaceutical processes. Novel printing technologies are becoming more and more popular as a manufacturing concept of personalized medications. Spectral Engines sensors can also be used for quality monitoring of printable medicines.

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