

20<sup>th</sup> International Conference and Exhibition on

# Pharmaceutics & Novel Drug Delivery Systems

March 18-20, 2019 | Edinburgh, Scotland

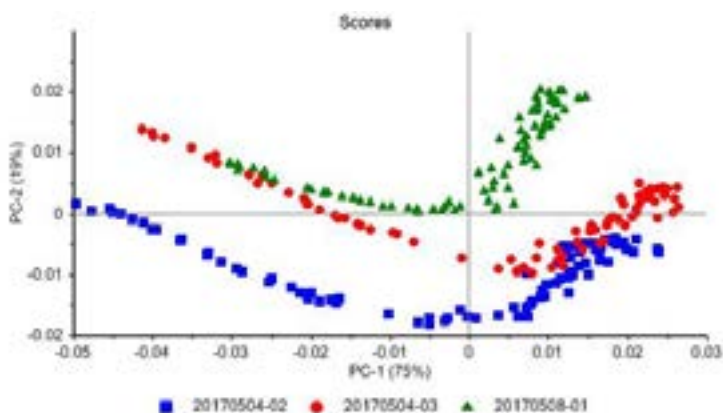
## Top spray granulation PAT monitoring by NIR: Calibration vs PCA trend approach

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**Statement of the Problem:** One of the main points of investigation to optimize a granulation is to precisely determine and monitor the process trend and the endpoint of each phase. The PAT systems give the possibility to operate a continuous, real-time process monitoring correlating the online response with the real measured parameters without the necessity of taking and separately analyze samples during process. The aim of this study was the feasibility to apply a NIR device to a fluid bed top spray granulation process to investigate the possibility to correlate the same NIR response to the moisture content and to the particle size distribution.

**Methods:** A placebo formulation was granulated by top spray using a fluid bed (Freund-Vector VFC-Lab3) equipped with a Viavi MicroNIR PAT-U device. The spectrophotometer is connected to the fluid bed with a welded flange. Two runs were performed. The load of dry blend was adjusted for the equipment capacity to achieve appropriate product movement. LOD was determined at regular intervals (5 min) using a thermobalance (Mettler Toledo MJ33). Particle size distribution was also determined using a graphical imaging device (Sympatec QicPic). Data were analyzed starting with the principal component analysis to locate the process trend, then the values were correlated to the samples collected to produce a calibration curve. The correlation proved to be very strong.

**Conclusion & Significance:** This study demonstrated the possibility to follow the process trend and to determine the phase endpoints both for moisture content and for particle size growth using a single PAT device. This could open up the possibility to apply this technology to other techniques, such as Wurster coating, fluid bed rotor powder layering and high shear granulation, and to implement a full integration of the NIR device with the machine software to get a complete automatic process control.



**Recent Publications:**

1. EMEA (2009) (Doc. Ref. EMEA/CHMP/CVMP/QWP/17760/2009 Rev 1) - Guideline on the use of Near Infrared Spectroscopy by the Pharmaceutical Industry and the data requirements for new submission and variations. (30pp.)
2. Pharmaceutical Analytical Sciences Group (2001) - Guidelines for the Development and Validation of Near Infrared (NIR) Spectroscopic Methods. (45pp.)
3. FDA (2004) – Guidance for Industry PAT – A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance (19pp.)
4. A.Liebermann, L. Lachmann (1981) – Pharmaceutical Dosage Forms (ed. Dekker).
5. Larry L. Augsburger, Harry G. Brittain et al. (2005) – Handbook of Pharmaceutical Granulation Technology (ed. Taylor & Francis Group, LLC)

**Biography**

Andrea Gelain took a master degree in Pharmacy and a master degree in Chemistry and Pharmaceutical Technologies. Worked for three years as a Pharmaceutical technologies researcher in Pharmaceutical Technologies department of the Milan Università degli Studi upon the formulation and preformulation of new conventional release and modified release solid dosage forms. Since 2016 works as Process Development Scientist in R&D department in Freund-Vector Corporation.

**Notes:**