Monitoring Fluid Bed Granulation Processes In-Line with Real Time Imaging

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Introduction

The pharmaceutical manufacturing platforms of fluid bed granulation is widely used to modify particle size. However the adoption of PAT to monitor and control this process is difficult, due to its dynamic nature. This study examines the efficacy of a particle characterising technology to capture particle images under dynamic conditions and to calculate particle size distribution data during fluid bed granulation.

Experimental Plan

The objectives of this study were to assess the ability to measure particle size distributions of fluidised particles.

- The acquisition of high resolution images during a dynamic manufacturing environment.
- The tracking of a fluidised bed process within a fluid bed granulator and the ability to monitor the wetting, agglomeration and drying phases of granulation.
Materials & Equipment

For in-line evaluation within a fluidised bed chamber, a placebo of Avicel and Lactose was granulated. Four granulation experiments were carried out in a laboratory scale fluid bed granulator (Glatt, model GPCG15). The formulation comprised of 33.33% Avicel, 66.66% lactose. The spray solution comprised of water and 5.5% PVP 90 with an addition rate of 220g/min using a Watson Marlow 505S peristaltic pump. Measurements were taken in real-time and the granulate growth per batch was evaluated.

Measurement of granulates was carried out using the Eyecon™ Particle Characteriser. The Eyecon™ was developed by Innopharma Labs as PAT (Process Analytical Technology) for the pharmaceutical industry. Its non-product-contact design allows it to be easily integrated into manufacturing equipment either in-process or at material outlets for real-time monitoring and control of particle size. The Eyecon™ was integrated onto a standard viewing port and acquired images of granules through the standard glass set-up.

Results & Discussion

Experiment: Fluidised bed evaluation

Figures 1a, b and c show the D10, D90 and Mean particle distributions during fluid bed granulation trials. All fluid bed granulation trials were circa 40 minutes in duration. Graphs illustrating the D10, D90 and Mean indicate the wetting, agglomeration and drying phases – typical of a fluid bed granulation process. Other D values (D25, D50 and D75) were also tracked and similar profiles were identified. During the process the technology successfully captured images, measured granulate size and tracked a typical fluid bed granulation process. The granulate size for all four batches reflected the typical granulate growth profile for a fluid bed granulation process – including the wetting, agglomeration and drying phases. The granulation growth trajectory and end points (as illustrated in figure 1a) could be monitored with this data. The variability between batches 1 and 4 versus 2 and 3 is most likely linked to variability in humidity levels during the trials as the dew point was not a controlled parameter and all other parameters remained fixed. These changes were confirmed through off line sieve analysis. It can be seen from the particle size data illustrated in figures 1a–1c that the dried granulate is of a smaller size compared to wet granulates earlier in the agglomeration process. This is to be expected when considering the removal of moisture and granule-granule attrition during the fluidised bed drying phase. All of the information presented in figures 1a–1c could be used to develop, model and control fluid bed granulation processes.
Figures 1a, b and c: Particle size results from fluid bed granulation platform.
Conclusions

The Eyecon™ particle characteriser successfully captured images and subsequently calculated particle size distributions for the sample materials in a rapid and accurate manner. As expected, there will be a degree of modification required as part of integration on new equipment types to ensure a representative and consistent sample presentation – which is critical to enabling accurate sample measurement.

It can be concluded that the Eyecon™ particle characteriser can be successfully integrated within typical pharmaceutical fluid bed granulators.

For More Information on Eyecon™ Please Contact

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