This presentation concerns the use of Lasentec® FBRM® in the manufacture of a bulk active pharmaceutical ingredient (API). Because API batches are manufactured in a highly regulated environment and can be worth up to $1 million each, accurate and effective analytical instruments are very important.

When development for a pharmaceutical process is finished, the New Drug Application package submitted to the FDA describes the quality attributes of the product based on the “bio” or validation batches. In the pilot plant, FBRM® statistics can be mapped to the quality attributes of interest (e.g., filtration rate, surface area, laser diffraction specification) to show that the physical characteristics of the product are identical before and after technology transfer.

Consistency in the bulk active is also critical. If the product drifts out of specified limits for a finished product physical characteristics test, FBRM® can be used to find the source of variability. In addition, measured FBRM® data and finished product data can be compared to look for correlations. Over a number of batches, the direction for process optimization emerges. A specification can be applied to an FBRM® statistic at different points during the crystallization to ensure the process is going in the desired direction.
In API production, an instrument may be left in a plant vessel for up to six months. At this duration, it is important to have continuous verification that the focal point position, scanner speed, and laser intensity are operating as they should. The built-in Calibration Verification System (CVS) of FBRM\textsuperscript{®} monitors for any change in the instrument that might affect its measurement.

It was concluded that FBRM\textsuperscript{®} has the potential to become an essential tool for bulk API manufacture. The success of FBRM\textsuperscript{®} has led to a mandate that all new crystallization equipment installed at Merck Sharp & Dohme production plants have a special instrument port in the dish of the vessel specifically dedicated to process analytical instrumentation. The FBRM\textsuperscript{®} probe is held in this port with a compression fitting, which allows easy adjustment of its position within the process.