instant measurements and avoiding the time delay typical of off-line analysis. The process control strategies take into account the attributes of input materials, the characteristics of process analysers and the achievement of process end points in order to ensure the desired quality of the final product. Measurement and science-based continuous improvement and knowledge management will continue to play important roles during the process and product life cycle.

PAT has become a "must have" tool during the design and operation of batch pharmaceutical and fine chemical processes.[2,3] PAT instruments are also relevant in the context of continuous manufacturing since they: (i) provide on-line measurements that are required to determine whether the process parameters are within the design space, (ii) can be used to shorten start up and shut down times and (iii) speed up the system response to disturbances and re-establish steady-state conditions faster than in uncontrolled operation.[2,4,5] The main PAT instruments used for monitoring and control of continuous crystallization processes are the focused beam reflectance measurement (FBRM), imaging, attenuated total reflectance Fourier-transform infrared spectroscopy (ATR-FTIR), ultraviolet-visible (ATR-UV/VIS) and Raman spectroscopy. A detailed description of these PAT instruments is presented in the following section.

9.2 Process Analytical Technology Instruments

9.2.1 Focused Beam Reflectance Measurement

FBRM is the most common *in situ* PAT tool for monitoring nucleation and crystal growth during crystallization processes.[2] The working principle of FBRM is laser backscattering: a rotating, high speed scanning infrared laser beam emanates through the probe window inserted in a slurry, which is reflected to the instrument whenever it hits a particle. By multiplying the length of time during which a continuous signal is reflected back to the probe by the velocity of the laser beam it is possible to calculate the chord length distribution of the measured slurry. Such chord length depends on both the size and shape of the particles. FBRM is an important sensor for the implementation of automated direct nucleation control (ADNC), a feedback control strategy that allows crystal growth and fines removal for continuous crystallization processes in mixed-suspension, mixed-product removal crystallizers.[4,6]

9.2.2 Ultraviolet-visible and Attenuated Total Reflectance Fourier-transform Infrared Spectroscopy

Ultraviolet-visible light (190 to 750 nm) can be absorbed by molecules containing valence electrons. These are promoted from their ground states to higher energy states and the magnitude of such absorption can be related to