Process Analytical Technology (PAT); What is PAT

Hyo-Jin Kim

College of Pharmacy, Dongduk Women's University

Process Analytical Technology is: a system for designing, analyzing, and controlling manufacturing through timely measurements (i.e., during processing) of critical quality and performance attributes of raw and in-process materials and processes with the goal of ensuring final product quality.

It is important to note that the term analytical in PAT is viewed broadly to include chemical, physical, microbiological, mathematical, and risk analysis conducted in an integrated manner.

A desired goal of the PAT framework is to design and develop processes that can consistently ensure a predefined quality at the end of the manufacturing process. Such procedures would be consistent with the basic tenet of quality by design and could reduce risks to quality and regulatory concerns while improving efficiency. Gains in quality, safety and/or efficiency will vary depending on the product and are likely to come from: 1) Reducing production cycle times by using on-, in-, and/or at-line measurements and controls. 2) Preventing rejects, scrap, and re-processing. 3) Considering the possibility of real time release. 4) Increasing automation to improve operator safety and reduce human error. 5) Facilitating continuous processing to improve efficiency and manage variability 6) Using small-scale equipment (to eliminate certain scale-up issues) and dedicated manufacturing facilities. 7) Improving energy and material use and increasing capacity.

In-line analysis has been a concern of the pharmaceutical industry. The Food and Drug Administration (FDA) recognizes these concerns and has recently taken measures, including issuance of a process analytical technology (PAT) guidance, to encourage pharmaceutical manufactures to employ real time monitoring control on risk based approach.

In this study, the quality of tegafur and uracil mixed final product, one of popular anticancer agent, was evaluated using in-line near infrared technique. Target product contains two different active ingredients tegafur and uracil, granulated individually before they are put together. Two active components are put into a plastic package with a certain ratio before the package is sealed. Because the ratio is very critical for medication, a special NIR analyzer was specially designed, for in-line monitoring of the mixing ratio (4:6) in the process on routine basis. The quantification of tegafur was performed and evaluated using partial least squares regression (PLSR), to develop a model for in-line monitoing.

The spectra were preprocessed with the Savitzky-Golay smooth and SNV transformation. PLS

was used to correlate the spectral changes based on the concentration of tegafur. The assignment of the NIR band in the in-line spectra of the final product could be performed using the known wavelengths of tegafur absorption. The regression vector spectrum was interpreted as related to tegafur and uracil, since tegafur was contributing positively to the loading around 1160-1185nm and uracil was contributing negatively to the loading around 1123-1126nm. The RMSEP of the PLS calibration model was 2.74(%), which proved to be sufficient to predict the tegfur content and provide in-line monitoring technology for risk based quality control based on PAT by FDA.