Process Understanding in Pharmaceutical Companies

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"PAT" and "analytical" are defined as shown in Table 1 in PAT Final Guidance (Guidance for Industry; PAT－A Framework for Innovative Pharmaceutical Development, Manufacturing, and Quality Assurance) issued by FDA in September 2004.

Table 1 Definition of "PAT" and "analytical"

The Agency considers *PAT* to be 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.

Recently PAT began to attract much attention partly because of the great progress of NIR technology, which enabled prompt measurement of the chemical and physical characteristics of materials in a non-destructive way. Although sensors such as NIR are essential to continuously or frequently monitor processes, sensors are not almighty. PAT is a system for designing, analyzing, and controlling manufacturing.

For example, content uniformity of tablets may be predicted with such a sensor. Such characteristics of tablets, however, can not be well controlled in the tabletting process no matter how much accurately and reliably they are measured. The primary objective of PAT use in the tabletting process is not the quality improvement of the batch but the improvement of QA level of the batch and quality improvement of the following batches. The objective of PAT use in a tabletting process is different from that of granulating process. Process analyzers to monitor granulating process should be paid more attention to. Shionogi developed such process analyzers without concept of PAT to manufacture quality products before FDA PAT guidance was issued.

As of October 2005, ICH Q8 Guideline (Pharmaceutical Development), ICH Q9 Guideline (Quality Risk Management) are at step 2. These guidelines include such concepts as Quality by Design, Continuous Improvement, Process Understanding, Design Space, and Risk Management

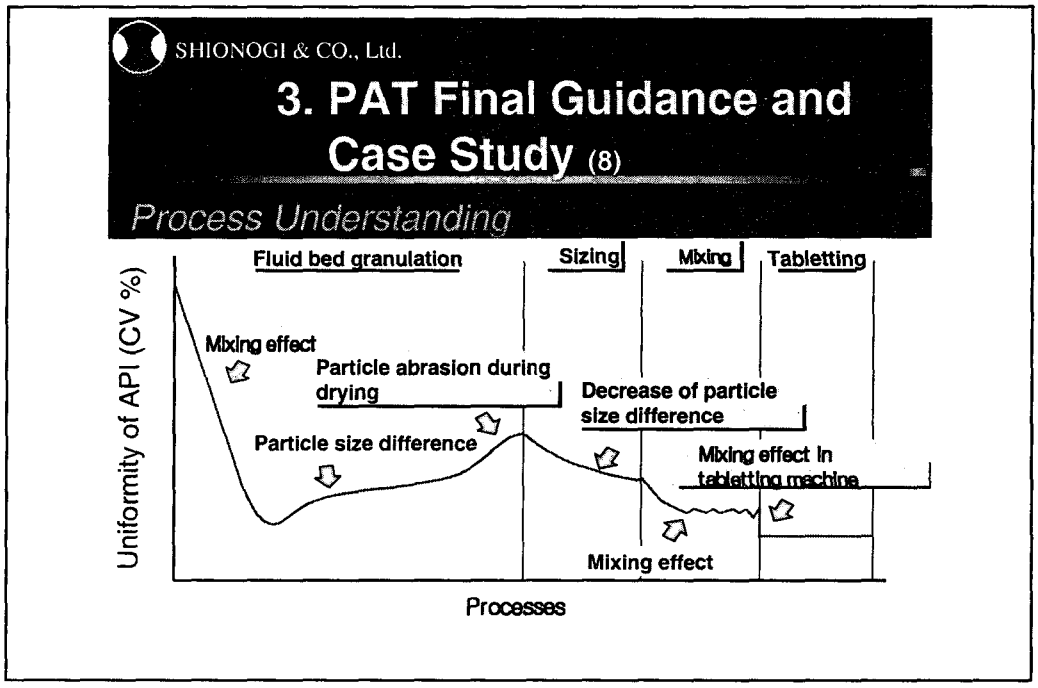
described in the PAT Final Guidance. It may not be an exaggeration to say that PAT must be discussed in the on-going and future pharmaceutical development. Although the PAT Final Guidance states "We would like to emphasize that any decision on the part of a manufacturer to work with the Agency to develop and implement PAT is a voluntary one.", PAT may be mandatory for the NDA for a new product to be marketed in the US in the near future.

The author's presentation entitled "Process Understanding and PAT Technologies " will include the following items with much emphasis on the optimization of manufacturing processes and PAT case studies in Shionogi.

1. S Objective of PAT
2. Status Quo of PAT overseas and in Japan
3. PAT Final Guidance and Case Studies

The above "PAT Final Guidance and Case Studies" will include the following items, which will be very interesting to the audience.

1. Understanding of granulation processes in terms of API uniformity



2. Technologies to Improve content uniformity of tablets
3. Optimization of particle size distribution of granules to improve tablet weight variation
4. Shionogi's new manufacturing technologies

4. PAT applications developed and used in Shionogi