

Proposed Process Analytical Technology Certification Program
for FDA Investigators and Reviewers

Course Objectives

On completion of this certification program, participants should be able to evaluate the adequacy and performance of current and emerging PATs. This certification will require a demonstrated understanding of the fundamentals, importance, and impact of PATs.

Participants will be able to demonstrate an understanding of:

1. The distinguishing characteristics of a PAT
2. The identification and use of PCCPs (process critical control points)
3. Suitability and validity of the statistics, chemometric, and instrumental approaches applied to PAT
4. Typical PAT applications and the associated capabilities and limitations of the methodology
5. Data handling, analytical, control and engineering tools and vocabulary relevant to PAT

Proposed Process Analytical Technology Syllabus for FDA Investigators and Reviewers - 6/13/2002

- 1) Background
 - a. Overview of PAT concepts and examples
 - b. Review of pharmaceutical unit operations
 - i. Reactions
 - ii. Separation (distillation, crystallization, extraction, chromatography)
 - iii. Mixing/Blending
 - iv. Storage
 - v. Transport
 - vi. Particle size reduction/Solids Handling
 - vii. Dissolution
 - viii. Packaging/filling
 - ix. Compression
 - x. Drying
 - xi. Cleaning and sterilization
- 2) PCCP definitions and identification strategies and impact on sensor selection.*
- 3) Measurement Systems
 - a. Figures of Merit: Robustness (interferences), speed, hysteresis, maintenance, reliability, (self) diagnostics, etc.
 - b. Continuous vs discrete
 - c. Process Sensors and Analysis:
 - i. Electrochemical
 - ii. Absorption spectrometry and optical sensors
 - iii. Uncommon spectrometric methods
 - iv. Separations/chromatography
 - v. Chemical imaging, optical, spectroscopy, XRD
 - vi. Temperature, pressure, flow, etc.
 - d. Pharmaceutical applications
 - i. Solids properties and their impact on PAT signals
 1. DR, scattering, etc. Merits and liabilities
 - ii. Other physical properties: density, viscosity, rheology, etc.
 - e. Sensor & sampler placement & maintenance, including effects on interferences
- 4) Sampling systems and issues: representative, effective, timely.
 - a. On-line vs. at-line vs. in-line
- 5) Data Handling*
 - a. Dimensionality (independent and dependent variables, multivariate systems)
 - b. Basic Statistics*

- i. Nature of Randomness
 - ii. Analysis of Variance
 - iii. Propagation of Error
 - iv. Figures of Merit: measurement uncertainty, precision, accuracy, limit of detection, dynamic range, sensitivity, specificity
 - c. Correlation and Regression
 - d. Chemometrics (specific items)
 - e. Pattern Recognition, Process signatures, and fingerprints
 - f. Database design and mining – informatics
 - g. Correlation between conventional and PAT methods as available
- 6) Process Control
- a. Automation vs. Statistical Control
 - b. Statistical Process Control
 - i. Statistical Sampling
 - ii. Attribute Charts
 - iii. Moving Range and Individuals Charts
 - iv. Components of Variation
 - v. Design of Experiments*
 - vi. Process Capability
 - vii. SPC of analyzers to assess on-going quality of data
 - c. Batch Automation*
 - i. Recipe management
 - ii. Within batch control
 - iii. Batch-to-batch control
 - iv. Characterization of batch trajectories and end points
 - v. Scheduling
 - d. Continuous Control
 - i. Feedback
 - ii. Feed forward
 - iii. Cascade
 - e. Model-based control
 - f. Control Implementation*
 - i. Distributed Control Systems
 - ii. Programmable Logic Controller
 - iii. Database Historians
- 7) Documentation e.g. DQ, IQ, OQ, PQ, and what should be included in each section
- a. Instrument enclosure design for clean-ability, e.g. slope of roofs
 - b. Power quality to analyzers
 - c. Maintenance of analyzers, e.g. proper PM procedures, PM frequency analysis*
 - d. Analyzer validation techniques including correlational analyzers
 - e. Calibration transfer and maintenance
 - f. Installation of analyzers, e.g. vibration effects on the analyzer, fiber optics

- g. Compatibility of materials in contact w/ the process, e.g. seals, adhesives in probes, etc.
 - h. Data security and audit trails
- 8) Wrap-up and recap
- a. Unit operations and suitable and/or common sensors
 - b. Basic capabilities and limitations of PATs
 - c. Analysis and control concepts
 - d. Case studies

Logistics

Pre-course preparation using supplied materials for review

Evaluation – based on review of published or generated PAT examples(s)

Course structure

- Didactic 8:30-3pm

- Team based case studies 3-5pm

- Homework – application of day(s) instruction

Practical training

- Washington – demo technologies on operations with data handling

- Tennessee – control technology with variety of sensors and controls

- Purdue – operation of sensor based line