ABSTRACT FOR PAT CERTIFICATION PROGRAM
9th Edition

NEW in PAT Certification IX:

1. ***Increased emphasis in QbD for new products applications and FDA PAI inspections***
2. ***New Emphasis in Continuous Manufacturing Developments-Hands-0n***
3. ***More Hands-On Participants' Involvement in Chemometric Model Development***
4. ***Umetrics SimcaP+ MVA as a Process Monitoring & Control Tool***
5. ***Biologics Case studies.***

MODULE I

PAT & QbD Regulatory Trajectories

3 hours web session by Prof Manuel Hormaza

- Part 1:
  - Why PAT?- A broad discussion of the regulatory map leading to PAT and QbD.
  - PAT FDA Guidance and New Perspectives & Concepts in Quality systems. A review of the FDA Critical Path Initiative and the resulting consensus standards efforts, modeled after ICH Q 8&9 and ASTM, guidelines and standard setting bodies.
- Part 2:
  - QbD Explained: CPP& CQA, QbD Flowchart, Design Space
  - Case Studies
  - Process Validation Guidance
  - FDA Regulatory Strategy

At the end of this session, the participant will be able to communicate what PAT/QbD are from a technical standpoint, why they are of paramount importance to the FDA and the lifecycle model for PAT/QbD.

MODULE II

Process Design and Understanding
(Practical applications in PAT & QbD) - 3 hours web session by Prof Manuel Hormaza

- Part 1:
    - PAT & QbD State of the Technology in PR and abroad; a review of the current global trends in industry and research in RTRT.
    - Case Studies in Dry Solids and Biotech (Cell Culture)
    - QbD preapproval inspection (PAI) readiness, CTD overview and discussion.

- Part 2: Real Time Release Testing (RTRT) & Continuous Manufacturing. Current developments (this topics will complement the hands-on section at UPR-M)

MODULE III

Process Measurements & Analysis

Spectroscopy Theory / NIR & Raman Webinar – 3 hours session by Prof. Rodolfo Romanach

This section is a broad discussion of the theory and practice of vibrational spectroscopy applied to pharmaceutical processes with an emphasis in the research and publications by Prof. Romanach in his UPR-M Pharmaceutical Spectroscopy lab.

Sampling technologies-(90% of error is in sampling) a review of sampling characteristics and best practices; what it takes to eliminate sampling error. Includes ASTM standard.

Two Days Hands-On (in Mayagüez)

Introduction- Prof Rodolfo Romanach
Spectroscopy Analyzers Hands-On– 2 hours session by Antonio Agullo, Instructor

A Hands-on, intensive, practice workshop with a variety of optical analyzers applied to modern pharmaceutical formulations.

- Analyzers (FT-NIR, NIR, Raman) parts and functions, calibration and operation allowing participants to interrogate prepared samples and to observe special effects in the spectral graphs produced. Use of different softwares to acquire and process spectra.

Chemometric Model Development Theory Hans-On– 6 hours session by Professor Rodolfo Romanach

- Identify NIR and Raman advantages and limitations for process understanding
    - Review Diffuse Reflectance and FT-NIR functionalities and applications from RMID to Content Uniformity and extrusion. Transmission applications: solvent recovery, crystallizations, Fermentation, etc.
- Discussion of particle size effects and other physical characteristics on NIR spectra.

Participants will learn the process of developing a chemometric model for quantitative and qualitative analysis with two spectral data sets. This will involve:

- FT from Dispersive NIR characteristics.
- PCA and PLS Theory

- Apply mathematical pre-treatment algorithms to the previously gathered data using popular software.
- Wavelength Range Selection
- Outlier Detection
- Number of Factors selection
- Model Error Evaluation and Validation

Second Day-Chemometric Model Development Workshop – 5 hours session by Professor Rodolfo Romanach & Instructors

Pretreatment, Calibration, Model Development & Model Validation

This lab includes a comprehensive session on calibration and model development. At the end of this session, the participant will be able to take spectra from samples using Raman and NIR analyzers and their software. Perform simple calibrations and model development techniques. Identify spectral outliers and determine different types of errors.

Participants will acquire spectra of samples with and develop with it two prediction models (PCA & PLS) using chemometrics. Participants will be divided in groups and will present their results and model development process. The exercise will be done with inputs from the professor and instructors. Presentations will be commented by the professor.

MODULE IV

Two Days Hands-On (in San Juan)

<u>Design Space, MVDA & DoE Applications (Experimental & Process Data Analysis)</u>

Design of Experiments (DoE)/ Design Space – 8 hours session by Prof. David Gonzalez
DoE concepts to optimize experiments and being able to describe the Experimentation Space, Design Space and Control Space of a multivariable system and the relationship between the variables.

Multivariate Analysis (MVA) – 4 hours session by Prof. David Gonzalez
Using MVA Applications such as PLS and PCA; Theory and hands on of MVA with SIMCA-P+ Umetrics software.

Multivariate Analysis in Chemometric Development – 3 hours session by Instructor Antonio Agulló

Using a spectral data set, MVA in chemometric model development will be compared with its use for process monitoring. Participants will follow instructor's explanation in SIMCA-P+ Umetrics software and review those aspects in which MVA's application for chemometrics differs from its use in process data analysis. The session will reinforce chemometric concepts learned in Module III with an emphasis on model error evaluation.

At the end of this session, the participant will be able to describe key aspects of the QbD Model and how it is applied to Process Development and Technology Transfer activities. Participants

will be able to differentiate between CQA and CPP, Design Space and Control Strategy. Participants would be able to understand advantages of Multivariate methods vs. univariate, and have a grasp for PLS and PCA applications and discern between their use for process monitoring and chemometrics.

MODULE V

REAL TIME RELEASE ROADMAP

3 hours session by Prof. Manuel Hormaza

Using as the basis IBS's Roadmap to RealTime Release™ (2004) this module overviews the Lifecycle approach to PAT processes, from feasibility to system maintenance; including updated ASTM standards covering Verification of PAT systems.

The module also covers a practical business and regulatory approach to PAT. It presents PAT/QbD as win/win tools to patient, product quality and sound business practice.

PAT projects must have a disciplined strategic approach that improves the bottom line as demonstrated with ROI calculations with benefits like improved cycle times, inventories, reduced non value added activities, such as CAPA investigations, regulatory exposure, reduced plant footprint, energy savings, etc.