The Development and Application of Micro-Analytical Tools for:

- Quality by Design (QbD), PAT,
- Process Intensification,
- Green Chemistry, etc.

‘the Competitive Edge’

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Quality by Design (QbD): A Global Implementation Perspective

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What is Quality by Design?

Systematic approach to development

- Begins with predefined objectives
- Emphasizes product and process understanding and process control
- Based on sound science and quality risk management

*From ICH Q8(R) Step 2*
FDA’s View of Elements of Quality by Design Approach

- The product is designed to meet performance requirements
- The process is designed to consistently meet product critical quality attributes
- The impact of formulation components and process parameters on product quality is understood
- Critical sources of process variability are identified and controlled
- The process is continually monitored and updated to assure consistent quality over time
PAT Tools

- PAT tools can be categorized as:
  - Process analyzers
  - Process control tools
  - Multivariate tools for design, data acquisition and analysis
  - Continuous improvement and knowledge management tools

- *PAT is more than just an analyzer!*
Example QbD Approach (Q8R)

- Target the product profile
- Determine critical quality attributes (CQAs)
- Link raw material attributes and process parameters to CQAs and perform risk assessment
- Develop a design space
- Design and implement a control strategy
- Manage product lifecycle, including continual improvement

Application of PAT tools
Examples of Process Analyzers in Manufacturing

- Monitoring only:
  - Assay by on-line measurement
  - Identity by on-line measurement
  - On-line particle size monitoring

- Monitoring and control:
  - Table compression weight check and adjustment
  - Endpoint determination of blending
  - Weight check and adjustment of powder filling operation
  - Adjustment of process parameters based on starting material attributes
Future Trends in Pharma?

- Widespread use of Quality by Design Principles
- Increased use of Process Analytical Technology (PAT)
- Use of Statistical Process Control in Manufacturing
- Move from batch continuous manufacturing
- Potential decrease in post-approval regulatory submissions
- Decrease in quality related product recalls
Cost and Benefit of QbD

Increased Resources
(e.g., development costs, organizational planning)

Decreased Expenses
(e.g. manufacturing costs, compliance costs)

QbD Implementation Progress

Initiate QbD Efforts
QbD Fully Realized

Manufacturing Costs
QbD Successes

- Industry is beginning to report cost savings from implementing QbD
  - Several talks at January IFPAC meeting in Baltimore, USA
- Publications reporting associated cost savings from
  - Reduced cycle times
  - Improve process capability
  - More efficient supply chain management

(e.g., Cogdill et al, J Pharm Innov, 2007, 2:38-50)
Challenges of Implementing QbD

FDA Challenges
- Defining and implementing new concepts
- Providing regulatory flexibility while assuring product quality
- Integration of review and inspection
- International harmonization
- Heavy workload and limited resources

Industry Challenges
- Industry’s continuous apprehension in sharing information with FDA
- Cultural changes needed in industry (and FDA)
- Communication across business units
- Management support
- More resources needed initially
Concluding Remarks

- Full implementation of Quality by Design is a Win-Win-Win outcome
  - Manufacturers – lessen regulatory burden and lower manufacturing costs
  - Regulators – lessen regulatory burden without sacrificing quality
  - Patients – increase in availability of high quality pharmaceuticals
Evolving Technology Areas

- Micro-Instrumentation
- Micro-Unit Operations for Processing
- High Throughput Experimentation
- Process Intensification
- Process Analytical Technology
- Production Optimization
  - Chemical Process Understanding
  - Fermentation Characterization
- Product Quality Improvement
MICRO-INSTRUMENTATION

- IMTeC PARIS
- CPAC PROJECTS
- ROME WORKSHOPS
- FDA PROJECT
- SIENA CONFERENCE
- AIChe IMRET
- PROCESS CHEM MEETINGS
- CCR NICHE
- ONAMI
- PROCESS OPTIMIZATION CENTERS (ITALIAN, UK-CPACT, PACIFIC NW, etc.)