PROCESS ANALYTICAL TECHNOLOGIES (PATs), APPLICATIONS AND BENEFITS WORKING GROUP

QUESTIONS TO THE WORKING GROUP

1. What is a common understanding (definition) of "PAT" in pharmaceutical industry?

2. What PATs for pharmaceutical applications are currently available, and will be available in the near future?

3. Why is the use of PATs lagging behind in pharmaceutical industry in comparison to other industries? Are there any perceived or real barriers for using PATs in pharmaceutical industry? If there are barriers, how can they be removed?

4. What role can/should PAT applications have in supporting the "quality by design" paradigm?

5. What public health and other benefits can be derived by using PATs in pharmaceutical industry, such as in the areas of

    - Process Understanding.

    - Level of Quality Assurance.

    - Manufacturing Efficiency.

6. Are there any disadvantages or limitations in using PAT applications in pharmaceutical industry?

7. Real time on-line quality assurance in lieu of laboratory-based testing, or end product testing, is perceived as the primary mechanism by which cycle time reduction occurs using PATs. How does this differ from the concept of parametric release?

8. Identify the essential or critical factors the FDA should consider in its effort to facilitate introduction of PATs (e.g. topics to be covered in guidance).

CHEMOMETRICS WORKING GROUP

QUESTIONS TO THE WORKING GROUP

1. What is the role of chemometrics and multivariate statistical methods in the application of PATs?

2. What are some of the chemometric and statistical tools needed for the use of PATs in pharmaceutical manufacturing?

3. What are some of the approaches that should be considered in the validation of chemometric based process analytical technologies?

4. What data are necessary to develop, validate, and maintain (e.g., re-calibration, root cause analysis of OOS findings, etc.) chemometric based process controls?

5. What are some of the issues encountered in the development, validations and maintenance of process monitoring hardware and software?

6. What PATs and chemometric tools are currently being used in chemical industries? Which of these can potentially be used in pharmaceutical industry?

7. What can be learned from the use of chemometric based PATs in fields outside of pharmaceutical manufacturing?

8. What approaches do you recommend for training Agency and Industry personnel in the analysis of chemometric based process controls?

PRODUCT AND PROCESS DEVELOPMENT WORKING GROUP

QUESTIONS TO THE WORKING GROUP

1. What considerations, during product development, are needed to ensure optimal application of PATs to realize "quality by design" through better understanding of processes and determination of performance-based process controls/end points?

2. What areas, from raw material identification/characterization to finished product manufacturing, are amenable to monitoring and control using process analytical technologies?

3. How do you anticipate PAT application will change the process for identifying critical process variables, their control, and establishment of product specifications?

4. What are some of the issues that arise during the scale up of pharmaceutical manufacturing, using PATs?

    - Do PATs help in the scale-up situations?
    - Do they cause problems?
    - Do they make scale-up transitions easier, and if so, why?

5. In some situations, PATs may be used only for certain specific unit operations within the overall scheme of a dosage form manufacturing. What are some of the advantages and disadvantages for doing so?

6. How can PATs be used to minimize, or prevent “out of specification” incidents?

7. How can PAT tools be used for predicting the performance of a drug product (e.g. dissolution) based on causal links and data based correlation?

8. Can PAT tools be used for predicting the stability of a drug product? If yes, what are the factors that should be considered prior to using them?

9. What factors should the Industry and the Agency consider while implementing the use of new PATs for already approved drug products?

PROCESS AND ANALYTICAL VALIDATION WORKING GROUP

QUESTIONS TO THE WORKING GROUP

1. What approaches should be considered for validating the use of new PATs for in-process control (of materials) during pharmaceutical manufacturing?

2. What databases will be necessary for validating PATs that will be used in pharmaceutical manufacturing.

3. What are some of the criteria for the validation of certain pharmaceutical manufacturing unit operations using PATs, for example:

    A. Blending.
    B. Granulation.
    C. Drying.
    D. Uniformity of active in dosage forms.
    E. Coating.
    F. Headspace analysis in sealed ampoules.
    G. Bioburden in solutions.
    H. Emulsification.

4. What are some of the principles involved in simultaneous validation of processes and analytical methods?

5. What considerations are needed to ensure that use of PATs will enhance overall quality assurance through integration of process monitoring and analytical measurement (of desired analytes) simultaneously?

6. Can some PAT tools be used in equipment cleaning processes and its validation?

    - What adaptations will be necessary for using PATs for equipment cleaning purposes?
    - What data will be needed to support use of PATs for equipment cleaning purposes?

7. What are some of the regulatory hurdles that may be encountered while changing from conventional process monitoring and control methods, to process monitoring and controls using new PATs?

8. What are your recommendations for training individuals who will need to evaluate new PATs that will be used by the pharmaceutical industry? What approaches do you recommend for such training purposes?

9. What are the key topics that should be included in a general regulatory guidance for making changes from laboratory test based process monitoring and control methods, to on-line process monitoring and controls, using new PATs?