INTRODUCTION

Leveraging Continuous Process Verification to Facilitate Faster Patient access

Ralf Gleixner
CASSS CMC Forum Europe, May 2016
Both EU and USA define three steps in the process validation framework

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<th>European Union</th>
<th>USA</th>
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<td><strong>Process validation:</strong> The documented evidence that the process, operated within established parameters, can perform effectively and reproducibly to produce a medicinal product meeting its predetermined specifications and quality attributes.</td>
<td><strong>Process validation:</strong> The collection and evaluation of data, from the process design stage through commercial production, which establishes scientific evidence that a process is capable of consistently delivering quality products.</td>
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<td><strong>Process characterisation (Development /evaluation)</strong> Small and/or full scale studies provide evidence that the manufacturing process design and controls allow to obtain a product of the intended quality.</td>
<td><strong>Process Design (FDA Stage 1)</strong> Defining the commercial manufacturing process based on knowledge gained through development and scale-up activities</td>
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<td><strong>Process verification</strong> Confirming that the final manufacturing process performs effectively and is able to produce an active substance or intermediate meeting its predetermined acceptance criteria, on an appropriate number of consecutive batches produced with the commercial process and scale</td>
<td><strong>Process qualification (FDA Stage 2)</strong> Confirming that the manufacturing process as designed is capable of reproducible commercial manufacturing.</td>
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<td>1. Design of a Facility and Qualification of Utilities and Equipment</td>
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<td>2. Process Performance Qualification (PPQ)</td>
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<td><strong>Ongoing process verification (aka continued)</strong> Documented evidence that the process remains in a state of control during commercial manufacture.</td>
<td><strong>Continued Process Verification (FDA Stage 3) (CPV)</strong> Assuring that during routine production the process remains in a state of control</td>
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Continuous process verification is a science and risk-based real-time approach to demonstrate that a process consistently produces material with the desired quality

• **Definition:**
  An alternative approach to process validation in which manufacturing process performance is continuously monitored and evaluated (ICH Q8).

• **Pre-condition**
  • Sufficient knowledge, and process understanding,
  • Extensive in-, on-, at- line controls and process performance and product quality monitoring

• **Enablers**
  • Process analytical technology application
  • Multivariate statistical process controls

• **Requirement**
  • Description of appropriateness and feasibility of continuous process verification strategy
    – Develop a “continuous verification validation scheme”?
    – Actual data to be available at the site for inspection?
Can Continuous Process Verification and the related Validation Scheme be introduced to Facilitate Faster Patient access?

**PPQ-to-Filing Timelines - Acceleration Approaches at BMS**
Marcus Boyer, *Bristol-Myers Squibb Company, USA*

**Demonstrating Effective Advanced Process Controls Using Continuous Process Verification**
Rohin Mhatre, *Biogen, USA*

**Continuous Process Verification: A Regulator’s View**
Martijn van der Plas, *College Medicines Evaluation Board (MEB), Netherlands*

**Panel Discussion – Questions and Answers (Facilitation: Jason Hampson, Amgen)**
Marcus Boyer, *Bristol-Myers Squibb Company, USA*
Niklas Ekman, *Finnish Medicines Agency, Finland*
Rohin Mhatre, *Biogen, USA*
Martijn van der Plas, *College Medicines Evaluation Board (MEB), Netherlands*