Agence nationale de sécurité du médicament et des produits de santé

Workshop on process validation

Session 2: Enhanced approach

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Process validation for process development following traditional vs enhanced approach

- Same objective:
  - To establish scientific evidence that a process is capable of consistently delivering a quality drug substance.

- Data expected:
  - Process evaluation
  - Process verification or continuous process verification
  - +/- Continued process verification

Process validation for process development following traditional vs enhanced approach

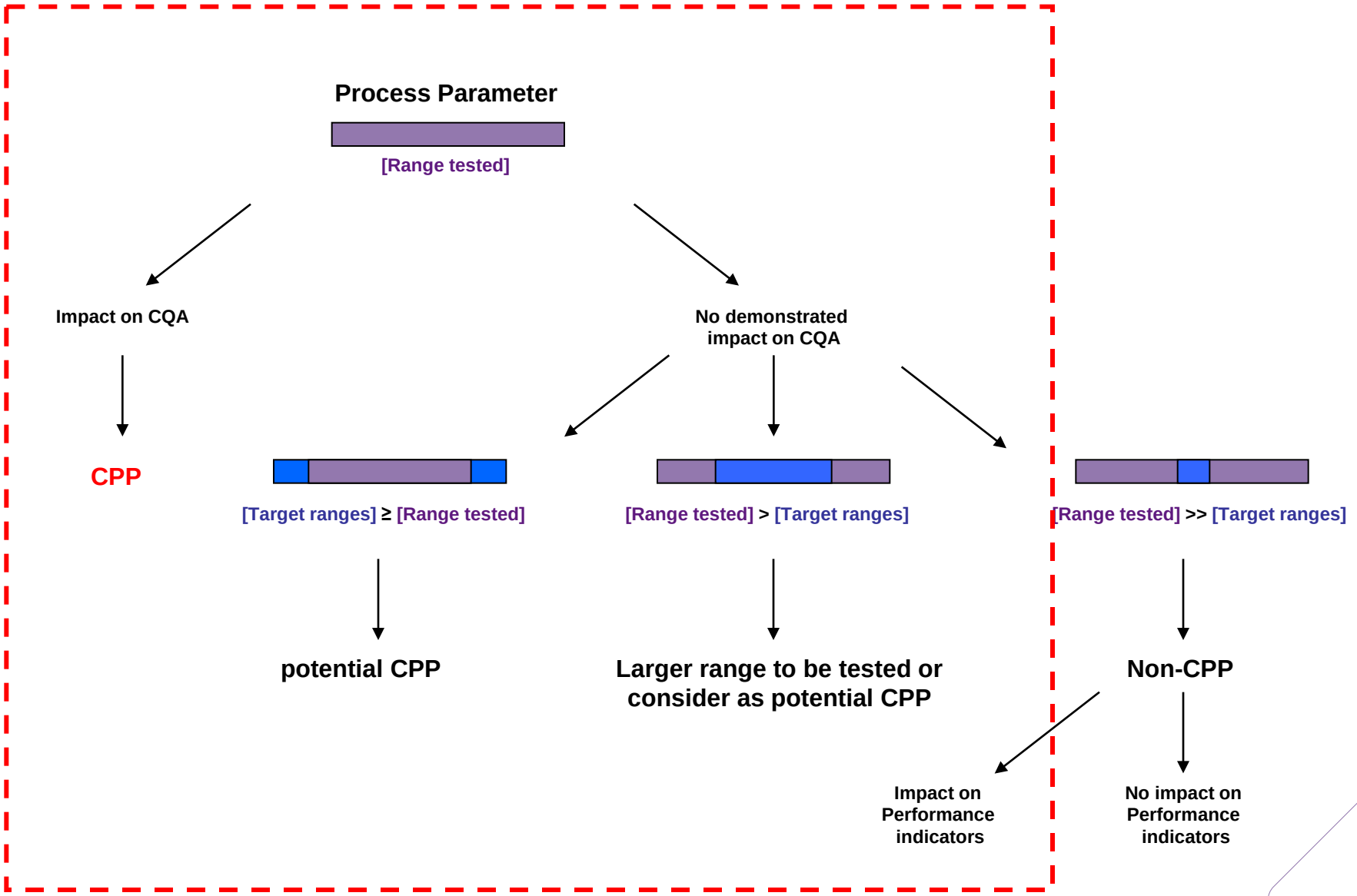
- **Process Evaluation: higher expectations**
  - Systematic approach using enablers (eg multivariate analysis, PAT tools, DOE, appropriate models including statistical model)
  - Demonstrated relationship between input/conditions (e.g. material attributes, process parameters) and output (e.g. CQA, Performance indicator)
  - Robustness demonstrated for selected steps (up to complete process), covering sufficiently large ranges
  - Demonstration of the suitability and predictability of scale down models (e.g. qualitative, quantitative, scale dependence)
  - Demonstration that working within design space delivers a quality drug substance.

  - *What additional studies would you consider in an enhanced approach versus a traditional approach?*
  - *How to evaluate and verify reliability/predictability of small-scale models for the upstream and downstream processes?*
  - *How to demonstrate validation of adaptive processes (e.g. with feed forward/feed back loops)?*

Process validation for process development following traditional vs enhanced approach

- **Process Verification:**
  - Compliance of complete process results to control strategy (including IPT and batch analysis) on appropriate number of batches manufactured at target
  - Alternative: continuous process verification
    - Science and risk based, real time approach
    - Controls of process performance and product quality in a timely manner (e.g. PAT tools)
    - *To be established upon accumulation of sufficient PV database?*

- **Continued process verification could include:**
  - *Verification in part performed on an ongoing basis after MA if proper evidence provided?*
  - *Included in CPV ?*
  - *Design space verification protocol?*



Expected to be included in process validation studies

Data to be submitted in MAA

TRADITIONAL APPROACH

ENHANCED APPROACH