# Session 3 Control Strategy Regulator´s Perspective

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# Examples of Challenges with Expedited Development Programs

- **Control strategy may differ…**
- Limited manufacturing and clinical experience
  - Too few batches to assess manufacturing consistency
  - Limited variablity seen in clinical batches
- Commercial scale validation activities may be ongoing
- Understanding of criticality & interactions not fully mature

- **… but products are still expected to be safe and efficacious (and to have a positive benefit/ risk ratio)**

# Control Strategy Expectations

- Regulatory expectations for a control strategy that assures product quality do not change for expedited development programs

- Utilize 21st Century Pharmaceutical Principles and CMC Development

  - ICH Q8: Pharmaceutical Development
  - ICH Q9: Quality Risk Management
  - ICH Q10: Pharmaceutical Quality System
  - ICH Q11: Development and Manufacture of Drug Substance

# Control Strategy Expectations

- Patient Focused Control Strategy

- Flexibility in what CMC information will be required for marketing approval will depend on factors such as the strength of
  - ➢ product and process knowledge
  - ➢ analytical capability
  - ➢ the quality system

  In the context of a risk-benefit assessment regarding risk of less CMC information vs. patient benefit

# Control Strategy Expectations

- Quality Risk Management though product and process knowledge gained through various mechanisms, including but not limited to:
  - in vitro data
  - animal data
  - clinical data
  - published information
  - prior knowledge
  - experience with higher doses than proposed where such experience exists to justify levels
  - small scale and QbD data
  - platform information

# Control Strategy Expectations

Increased knowledge of quality attributes and process can be used to support control strategy flexibility, including acceptance criteria  and process parameter ranges outside of manufactuing and clinical experience

# Risk Mitigation for Control Strategies

- Applicant should address residual risks of control strategy and can include consideration for in-process testing, lot release, stability, comparability, monitoring, control of raw and starting materials, etc

  - Expedited development programs can, at the time of approval, lead to increased risks associated with element of the conrol strategy (e.g., uncertainty on the criticality of attributes, their control by the manufacturing process, and analytical capability) which will need to be addressed

# Examples of Risk Mitigation for Control Strategies

- Potentially more attributes, process parameters, and assays in the application control strategy. The control strategy can be revised when more knowledge is gained.
  - e.g., Consistent impurity removal by the manufacturing process, capacity of purification process to remove impurities as shown in validations or batch testing, updated criticality assessment showing less criticality for certain attributes

# Questions

- What control strategy activites can be front loaded for expedited development programs vs. a standard development program.
- What would a post-approval change managment plan for control strategy changes ( IPC´s, attributes tested, limits applied,  etc.) look like?
- Should certain performance based and intelligent control strategies be introduced into control strategies for standard CMC development programs before introducing into expedited development programs