Expectations for Updating Quality Data for Clinical Trial Drugs

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Willem Stevens Ph.D., Chief
Plasma Derivatives Division
Centre for Biologics Evaluation
Biologics & Genetic Therapies Directorate

Rationale

- Within the framework of evaluation for Clinical Trial drugs, decisions are made appropriate to the developmental stage of the investigational drug based on the available information and the intended use in Clinical Trials.
- When these parameters change, it is appropriate to re-visit the ongoing applicability of the decisions made.
- Based on the extent of the changes made filing of amendments or new applications may be warranted.
Context for Review

- What is the intended use, patient population, size of trial?
- What is the phase of trial and stage of development of the drug?
- What is already known about the product?
  - Previous trials
  - Drug development
- Is product type/class known to have specific quality concerns (e.g. problematic impurities, previous safety issues)
- What is the level of experience of the manufacturer and the degree of their involvement in drug development?
- Is there enough data present to assess the safety of the drug from a Quality (CMC) standpoint and is the data supportive?

Amendments (Pharmaceutical DS)

- Introduction of new ingredients (including those removed in the manufacturing process).
- Identification of a new impurity or degradation product.
- Removal or relaxation of a Drug Substance specification.
Amendments (Pharmaceutical DP)

- Introduction of new ingredients (including those removed in the manufacturing process).
- Changes to the manufacturing process for sterile products where the sterilization process has changed.
- Removal or relaxation of a Drug Substance specification, or replacement of a test method with a less sensitive one.
- Where Clinical trials change Phase, updated Quality (CMC) information should be filed to conform to expectations for increased understanding and control through development. Where templates are different, this could trigger filing of a new application.

Amendments (Biologics 1)

- In addition to those described for Pharmaceutical drugs, amendments are expected for extension to shelf life where the original expiry dating was < 18 mo. and where modifications to existing facilities are proposed.
- For more significant changes, a new Clinical Trial Application may be required.
Amendments (Biologics 2)

- A new Clinical Trial Application may be required when:
  - A new facility is used for fabrication
  - Changes are made to biological starting materials
  - Changes are made to expression systems
  - Changes are made to the purification process
  - Changes are made to the dosage form (e.g. lyo to liquid formulation, or to final product strength)
  - Significant changes to DS or DP specifications

Plenary Discussion: Amendments

- Concerns?
- Unresolved issues?
- Additional Clarification?
- Experiences to Share
Thank You!