Roundtable Session 2 – Table 15 – Strategies for Leveraging Clinical Stability Data for Commercial Shelf Life

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Abstract:

Strategies for leveraging clinical stability data for commercial shelf life can be critical in accelerating a biological product to market. The justification will vary depending on the drug substance and drug product types, their complexity, manufacturing processes, CCSs, and analytical comparability between the clinical batches with the intended commercial process batches. This round table intends to discuss with regulators and industry strategies that can be successfully used across the product lifecycle while meeting global regulatory expectations by leveraging clinical stability data for commercial shelf life

Questions for Discussion:

- What are the key considerations/justifications for leveraging clinical stability data for commercial shelf life?

- What products/programs could apply the strategies leveraging clinical stability data for commercial shelf life?

- What is the data package expected for leveraging clinical stability data for commercial shelf life?

- what are the challenges and regulatory expectations for leveraging clinical stability data for commercial shelf life?

Minutes:

Ideally the goal is to leverage clinical batch stability data as part of the scientific justification and with PPQ batches often with limited stability data to set shelf life. The justification of batches being used as primary batches is based on analytical comparability, clinically relevant specifications, and demonstrated as being representative of the intended commercial product. Primary batches may be GMP batches intended for human use but also may be technical or engineering batches as long as they are deemed representative. Leveraging clinical stability is likely to be more critical to the strategy of setting the commercial shelf life for ATMP products because of the minimal number of batches manufactured.

There is opportunity to apply statistical modeling to the clinical batch stability data to support extrapolation as part of shelf life setting. In order to use this approach, an assessment of the model and data should be done to confirm a low risk for extrapolation.

Challenges of leveraging clinical data include

- CMC changes between clinical batches and PPQ and commercial batches.
- Use of clinical batch data for a marketing application in a country where clinical studies were not conducted
- Country-specific regulations regarding real time stability data from intended commercial batches

Industry experience of using clinical batch data

- Leveraging stability from a clinical batch of one strength to support introduction of a new strength (same DS, DP process, container closure) for commercial.
- Using stability from a product with one fill volume to support a new fill volume. The clinical stability presentation should be considered worst-case to apply to the fill volume change.
- Applying stability from clinical batch to the commercial batch with a change in formulation (only change in amounts, not excipients) with justification that the change in excipients does not have clinical impact.

Challenges for leveraging clinical stability data for commercial shelf life

- Using clinical stability data to support commercial shelf life when clinical studies have not been conducted in the country where the initial marketing application is being submitted.
- Certain Health Authorities can be challenging because of the requirement for real time data of the intended commercial product (e.g. select LATAM and Asian markets)

Predictive Stability Strategy when clinical stability cannot be leveraged

- Require verification that the model is accurate and is scientifically justified that the model is transferable from the current data set from clinical lots to the data set for the commercial product batches.