Roundtable Discussion Session 1 and 2 – Table 5: Stability Testing

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Abstract:

Stability testing should generally follow ICH stability guidance

"The design of the formal stability studies for the drug product should be based on knowledge of the behavior and properties of the drug substance and from stability studies on the drug substance and on experience gained from clinical formulation studies. The likely changes on storage and the rationale for the selection of attributes to be tested in the formal stability studies should be stated."

However, CGTP pose unique challenges and opportunities

A risk-based (and data-driven) approach should be used to determine specific testing for CGTP

Testing should cover shipping, storage, and holding of CGTP at all stages of manufacturing and use

Discussion Notes:

- Photostability: Typically not done for cellular products
- Selection of batches: How do you get stability data from patients where batches are precious?
- Batch selection is product-specific
- Early development should utilize engineering runs to gain manufacturing experience and product knowledge
- Stability protocol should be ready before patient enrollment to allow for a shift to patient samples later in development
- Container Closure System:
- Utilize container closure system proposed for marketing
- With limited material - utilize worst case conditions (surface area/volume) to design stability program
- Specifications and Product Characterization: Testing should include critical quality attributes of the drug product that are susceptible to change during storage and are likely to influence quality, safety, and/or efficacy
- Storage: Testing should include evaluation of stability during
- Long-term storage
- Drug product in-use period (in-use stability data to be collected as part of the in-use compatibility evaluation)
- Testing should include attributes of the drug product that are susceptible to change during storage and are likely to influence quality, safety, and/or efficacy
- Critical Quality Attributes (CQAs) for CGTP
- Visual appearance - expectation of 100% inspection for all drug product
- Particle observations

- Extrinsic particles - actionable/ should raise an alarm for the DP
- Intrinsic particles - important to minimize these and ensure homogeneity of final drug product; it is important to document and understand the safety impact
- Viability
- Industry practice is assessment of membrane damage
- Healthy authority expectation of >70% viable cells
- (Product-specific) Potency - Reflective of the mechanism of action of the drug product
- Other important measures of “cell health” may be more appropriate
- Apoptotic index via staining of apoptosis markers
- Outstanding question of what is needed to bridge testing to clinical outcome
- Hold-times:
- Intended to evaluate the worst-case conditions for DP hold-times
- The goal is to dose as fast as possible, but collect data to support longer hold times
- Drug product source:
- Sample should reflect representative clinical final drug product (fresh or thawed product as appropriate)
- Additional considerations for in-use testing:
- Control strategy should include careful consideration of time to manufacture
- To define time zero for the fresh product
- All relevant tests should be performed
- May be necessary to leverage these studies in comparability assessment in place of accelerated stability conditions