Roundtable Session 1 - Table 11: In Use Stability and Compatibility Testing : Microbial Challenge Studies and Requirements

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Abstract:

Microbial challenge studies are performed to evaluate the microbial growth potential during the reconstitution and preparation of the Parenteral biological products after breach of sterility. The results from the microbial challenge study along with the in-use physicochemical stability study are used to define the hold times and storage conditions during the dose preparation and administration. This information must be clearly stated in the pharmacy manual for clinical products and Prescribing information for commercial products to ensure the patient's safety.

The FDA requires that storage times over 4 hours at 2-8°C/room temperature prior to administration must be supported by microbial challenge study data. Since in-use microbial risks are not equal for all products due to product difference as well as dose preparation and administration environment, proper study design and data interpretation are critical for assigning appropriate in-use hold times. However, there are no formal FDA guidelines on how the microbial challenge study should be performed. The industry is leveraging FDA presentations, review comments, information requests, publications and working groups to gain a better understanding of the study design and data interpretation.

Questions for Discussion:

1. What are the current regulatory requirements for microbial challenge studies from health authorities in different countries/regions?

2. What is the current industry experience on leveraging platform approach to justify longer time limits for new clinical stage products?

3. What are the considerations and challenges of designing a microbial challenge study? Do you design and perform the risk-based microbial challenge study?

4. How do you interpret the data from microbial challenge studies and assign in-use hold times in biological product labels?

5. What are the current regulatory requirements and the industry experience on performing microbial challenge studies for gene therapies?

Notes:

- Current regulatory requirements for microbial challenge studies are not explicit.
- Generally follows USP <51>, however early stage programs does not follow any specific guidance.
- One of the challenge is that there is no specific information on the way clinical studies are conducted wrt hold time etc
- So far, no specific question from agencies on the microbial challenge studies for early stage (Ph1/2) studies per participants

- Determination of sub vis particles and potency is an expectation for in-use studies, regardless of agency query or not
- One of question from a participant was that if in-use study at 30C in one ICH region can be leveraged for 25C for another ICH region as worst case? No specific experience from the participants
- Some companies filed microbial challenge data for IND stage also. However, the concern is that final dose may not be available at the time of IND filing and needs to repeat in late stage
- Some companies consider duration of the administration for in-use studies and include a safety factor
- What are the considerations when a on body pump is used for administration? Should a temperature close to body temperature is used for in-use study temp in that case?
- What comes first, biocompatibility or microbial challenge? General consensus is biocompatibility.
- What happens when biocompatibility is established, and a site wanted to change to another component for administration? Do you need to repeat the study? Consensus is yes. Perhaps it makes sense to delay the study till components used in the study is final via biocompatibility studies.
- In-use study requirements for gene-therapy is not different from standard biologics for now.