Table 57: In-use Stability: How to Develop a Plan for your Product

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SCOPE:
The preparation of drug product for patient’s dose in a hospital setting often involves diluting a liquid product or reconstitution of a lyophilized product with proper diluents (such as sterile water for injection, 0.9% sodium chloride solution, or 5% Dextrose in water, etc). During the drug administration process, the diluted product, or even undiluted drug product for neat injection, may come into contact with different materials, such as infusion bags, in-line filters, etc.

Drug product manufacturers need to demonstrate the compatibility of drug product with administration material, and the stability of a drug product after reconstitution, dilution, or under so called “in-use conditions” is not compromised. ICH Q1A (Stability Testing of New Drug Substances and Drug Products) states “Stability testing of the drug product after constitution or dilution, if applicable, should be conducted to provide information for the labeling on the preparation, storage condition, and in-use period of the constituted or diluted product”.

This round table discussion covers common practices and challenges during the in-use stability study, as well as regulatory expectation or requests on this topic.

QUESTIONS FOR DISCUSSION:

1. How does your company develop the in-use stability plan? What are the inputs, what are the studies that are typically done and how are they designed?
   a. During early stage development (tox, Phase 1)
   b. During late stage clinical development (Phase II and III)
   c. What administration components do you include in the compatibility study? (Infusion bags, filters, closed system transfer device (CSTD), any others?)

2. What data (i.e. the number of DP batches, study duration, etc) are usually included in regulatory submissions?
   a. During IND (Phase I, II, or III) stage?
   b. In BLA or NDA application

3. What are the typical challenges? What questions have been received from regulatory authorities?

4. When does your company conduct microbial challenge studies for in-use conditions? What are the factors will impact the decision on microbial challenge studies?

5. How about the microbial challenge studies for legacy or marketed products? Under what condition such studies will be repeated or conducted to bridge historical gap?