Table 28: Linking Process Variability and Clinical Experience to Support Establishment of Clinically Relevant Specifications

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SCOPE:

The establishment of clinically relevant specifications has been an area of substantial focus and debate for biological products across the industry and health authorities. This discussion will explore approaches to define appropriate, clinically relevant, specification acceptance criteria to support registration of these products. Approaches and challenges to broaden product attribute ranges during clinical development will also be discussed.

QUESTIONS FOR DISCUSSION:

1. Examples of how to vary and/or broaden attribute ranges of clinical materials
2. Considerations for producing clinical material at process targets vs. varying within the allowable process parameter ranges
3. Challenges related to incorporation of clinical materials with broader attribute ranges (e.g. perceived risk to clinical study, clinical material supply strategies, limited number of lots…)
4. Considerations for incorporation of drug substance and drug product clinical materials near the end of shelf-life into the clinical studies
5. Alternative approaches to support clinical relevance (e.g. tox, literature, in vivo, in vitro studies…)
   a. Acceptability of extrapolation from ranges of product attributes included in studies
   b. Considerations for modifications that are known to occur in vivo
6. Examples of established links between material attributes and measurable clinical outcomes.