Table 4: Stability-indicating Methods

Scope

Pharmaceutical development is a complex and challenging process that requires careful attention to safety, efficacy, and quality. In the early stages of development, forced degradation studies are conducted to assess product stability, developability, and to identify critical quality attributes (CQAs) of the product. During product development and clinical studies, degradation pathways are elucidated, and the drug substance (DS) and drug product (DP) are tested during stability studies as part of the control strategy (CS) and to provide a shelf-life statement. To ensure reliable data interpretation, stability indicating methods are needed, which allow for the detection of at least the active pharmaceutical ingredient (API) degradation.

In this roundtable, we will discuss what makes a method stability indicating. Is API content and potency determination and regression analysis enough? Should evolutive profiles play a role? To what extent do the changes in profile need to be understood thinking of peak identification and peak purity? Additionally, we will consider how such methods should be validated. Is validation for content decrease enough, or should validation samples be stressed? Should precision and accuracy be determined in stress samples as well?

Discussion Notes

- What makes a method stability-indicating?
    - A method that measures the API and is able to show change in the attribute is considered stability-indicating.
    - Assessment whether a method is stability-indicating is done by performing a forced degradation study.
- Do we need stability-indicating methods in characterization?
    - Yes, we need stability-indicating methods also in characterization. In characterization they are used to investigate degradation pathways of the API. This can also done by a forced degredation study.
    - Is a forced degradation study to assess degradation pathways useful?
        - Yes, such a study is useful to investigate possible degradation products. However, long-term stability studies at real storage conditions may induce also different degradation routes, yielding additional peaks /changes in your results. Therefore, forced degradation studies cannot replace the long-term stability study.
- To what extend do the changes in the profile need to be understood?
    - Examples were provided for insulin and antibodies. Consensus is that you need to characterize each peak, also peaks appearing during stability studies.
- How should stability-indicating methods be validated?
    - A validation should include an assessment for specificity to show that the signal/result changes when a product is degraded. This can be done by inclusion of a stressed sample.
    - Also, precision using a stressed sample is performed.