Summary - Stability Considerations for Planned or Unplanned API Process Changes

Changes can be classified (e.g. as minor or major) depending on the nature and extent of the changes and the effects these changes may impart on the process." A minor process change may be defined as a change that has no impact on registration or validation, and little or no impact on product quality. A minor process change should not require major testing or development efforts such as generation of supportive stability data. If stability data are needed, then the change should be categorized as major.

The evaluation of a major process change may require development support, including the collection of stability data. Examples of a major change could include, but are not limited to, the following:

- Process scale-up
- Implementation of a revised process
- Implementation of a new rework procedure
- Change in packaging or packaging supplier
- Change in storage conditions
- Change to existing process equipment (i.e. repair, modification, replacement not like for like)
- Transfer of the process to a new or different site
- Change in critical raw material production process or supplier

If a change has the potential to impact the regulatory process description, then the impact on API stability should be evaluated and documented. For example: a site change, a change to the primary package or a change in the storage conditions may require a stability study.

If a change has the potential to impact validation, then the impact on stability should be evaluated and documented.

If a process change results in a revision of the registered process description, supporting stability data may be required. European Medicines Agency (EMEA) requirements base stability protocol design on the type of process change.

A Type I Variation only requires supporting stability data for changes in API retest date or storage conditions. A Type II Variation refers to changes that affect API attributes that have an impact on stability. For changes of this type, accelerated and long-term stability data are required.

Stability studies can be initiated after batch release if the data will be used to fulfil annual stability commitments or if the data are for information only (e.g. analysis of a proposed package change or some other non-process related change).

If stability data supporting a deviation are not consistent with historical stability data, then the affected batches may require rejection, rework or reprocessing prior to release.

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