__ Was the API prepared at approximately the same batch size (e.g. within +25% linear scale of the validated batch size)?

Requirements, acceptance criteria, and conclusions for the homogeneity study may be included in the process validation documents, or may be presented in separate documentation that is referenced in the validation documents.

**Materials to be tested**

__ Homogeneity shall be demonstrated for finished APIs unless otherwise justified and documented.

__ The need to show homogeneity of isolated critical intermediates should be considered on a case-by-case basis depending on how the intermediate is used in subsequent processing. In general, studying the homogeneity of an intermediate is of less importance than that of a final

API, especially if the intermediate will be dissolved in the next step of the processing. If homogeneity of the intermediate is critical to the quality of the final API prepared from it, demonstration of intermediate homogeneity should be considered.

__ Homogeneity testing is typically not needed when the API is a liquid, because of the inherent homogeneous nature of such materials.

**Selection of Test Methods for Examining Homogeneity**

Three measurements are typically considered for a given homogeneity study: one to demonstrate chemical homogeneity, one to demonstrate physical homogeneity (if appropriate), and one to demonstrate the effectiveness of the drying process (if appropriate). Appropriately chosen analytical tests in these categories usually eliminate the need to perform other analytical tests to show homogeneity.

__ Chemical Homogeneity: Process impurity testing is generally the preferred analytical methodology for examining chemical homogeneity of small molecules, but other analytical techniques may be used. For large molecules, the consistency of the profile of heterogeneity of product-related molecular variants is demonstrated by appropriate techniques.

__ Physical Homogeneity: Evaluation for physical homogeneity may include tests such as those for particle size distribution, crystal form uniformity, and/or bulk volume. Where physical quality attributes have not been established for the API, physical homogeneity need not be demonstrated. If this is the case, it should be explained in the validation protocol.

__ Effectiveness of Drying: This may be important because residual solvents (including water) are considered process impurities. This assessment is especially important for higher risk cases such as vacuum tray driers used for static drying operations. Attention should be focused on either the last solvent used in the process, and/or the solvent that is most difficult to remove from the API.