Summary - Demonstration of Active Pharmaceutical Ingredient Batch Homogeneity

This procedure provides guidance for performing a homogeneity evaluation in support of API process validation.

- Materials to be tested
- Selection of test methods for examining homogeneity
- Sampling plan – when to collect samples, from what locations, and the of samples
- Selecting acceptance criteria for evaluating homogeneity test results.

Homogeneity is the acceptable distribution of chemical and physical properties within a batch, based on predefined criteria. The intent of examining homogeneity during the validation is to demonstrate that the quality of a sample collected from any location within a batch is representative of the quality of the entire batch.

For large molecules the evaluation of homogeneity must consider the consistency of the profile of heterogeneity of product-related molecular variants. This profile should be consistent throughout a batch and similar between batches.

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.

Sampling should target potential in homogeneity. An API process generally prepares a material that is a single substance rather than a mixture of materials (such as that found in a drug product), and a well-mixed API batch is typically obtained near the end of processing. Operations that potentially introduce inhomogeneity in APIs are readily identified (examples include collection of caked material from a crystallization tank, non-agitated washing of filter cakes, and non-agitated drying of filter cakes), so sampling and analytical testing may be targeted at investigating suspected potential for inhomogeneity.

For an API quality attribute that is considered acceptable when it conforms to a limit or range (as is true for many physical properties), homogeneity may be established by demonstration that each sample of the API lot conforms to the limit(s) for that property. Analytical test results that are normally reported as "Meets Test" or "Acceptable" for chemical properties are not suitable for evaluation by statistical methods.

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