

- Brief description of product, including product name, dosage form, and strength where applicable;
- Master manufacturing instructions or Device Master Record (DMR) to be validated;
- Brief description of process with a summary and/or process flow diagram of critical processing steps to be evaluated and critical parameters to be monitored;

Acceptance criteria for the following:

- Acceptability (meeting established critical quality attributes and specifications);
  - The number of consecutive successful validation batches/lots needed to show consistent control of the process.
  - Equivalency to existing drug products (where applicable) by comparison to previously produced batches/lots (commercial, development, or biobatches).
  - Requirements to conduct homogeneity and hold time studies, if applicable;
- Sampling plan, including type, amount, and number of samples, together with any special sampling or handling requirements.
  - Critical process parameters and operating ranges, including justification for these Ranges.
  - Calibration of any critical equipment used specifically for the validation studies (e.g., one-time studies on validation batches/lots using portable equipment, measuring equipment);
  - Plan for the number of batches/lots to be put on stability, if any; and
  - Methods for recording and evaluating results (e.g., statistical analysis).
3. On-Line or In-Line Monitoring may be used, in lieu of discrete sampling (e.g., to demonstrate homogeneity or acceptance criteria).
  4. Homogeneity should be demonstrated throughout the batch, when required by the validation protocol.

A sampling plan for the homogeneity study should be provided that justifies the number of individual locations and the number of samples to be taken from the product batch [e.g., for blend uniformity]. The bulk should be representatively sampled based on product type (e.g., aqueous solution or solid dosage), mixing container geometry and process (e.g., mixing mechanism) on completion of process step. Additional sampling on completion of discrete critical steps may also be

- In-process assay of bulk tank and bioburden testing, where applicable;
- Environmental conditions (e.g., temperature and humidity control, air classification, pressure differentials), where applicable;
- Removal of oxygen, where applicable;
- Dose and/or content uniformity;
- Fill weights or volume controls;
- Moisture content, where applicable; and
- Foreign matter including particulates.

If validation is being carried out as a result of a change to an existing process, documented justification should be provided in the validation protocol if any of the above applicable parameters are not to be assessed.

Media fill, environmental monitoring, and moist heat terminal sterilization process studies that support the process being validated should be referenced in the validation protocol.

- 14.** Dry Powder Inhalers -validation should include evaluation of the mixing process (where applicable) and filling process.

In addition to the general protocol requirements, the process validation protocol for dry powder inhalers should include assessment of, at least, the following:

- Emitted dose uniformity; this should assess both inter and intra inhaler dose uniformity;
- Fill weight or volume and number of deliveries from the container;
- Airflow resistance;
- Aerodynamic assessment of fine particles using a multi-stage impactor;
- Compliance with finished product specification, including any microbiological requirements; and
- Comparison with the previously produced lots (e.g., commercial, clinical, development, or biobatches).

Device Parameters:

- Robustness of Process Capability of component manufacturing and finished device assembly processes demonstrated; and
- Compliance of component(s) to specification including extractables data for components in the drug/airway path and in intimate mucosal contact. Validation should be initiated as the result of a component change.

Drug/Device Combination Parameters:

- Respirable Fraction of delivered dose.

If validation is being carried out as a result of a change to an existing process, documented justification should be provided in the validation protocol if any of the