Potential Critical Parameters for Process Involves in Formulating Solid Oral Dosage Forms

**Regulatory Basis:**
FDA Quality Systems Regulations

Reference: FDA CFR - Code of Federal Regulations Title 21

**General Discussion**

This document provides an overview of potential critical process parameters for the manufacturing of solid oral dosage forms.

Solid oral drug products come in a variety of dosage forms frequently with common steps and equipment. The potential critical process parameters are often the same from process to process. This document provides an overview of process steps and typical equipment involved in manufacturing of solid oral dosage products and notes what might be critical process parameters associated with these process steps and equipment.

**Solid Oral Dosage**
Critical process parameters (CPPs) and critical quality attributes (CQAs) that need to be monitored during process validation for a bulk solid oral dosage formulation depend on its presentation (e.g. compressed tablet, coated tablet, capsule) and its drug release characteristics (immediate release-IR or modified release-MR). The following table of process parameters and attributes can be used as a guide for use in process validation. Each application should be evaluated on a case-by-case basis to determine which parameters and attributes are critical.

 

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| Process Step | Type (Examples) | Potential Critical Process Parameters | Potential Critical Quality Attributes |
|---|---|---|---|
| | Cone mill (e.g., Comill) | • RPM<br>• Screen size<br>• Feeder speed<br>• Impeller (blade) type<br>• Gap for impeller | |
| | Hammer mill (e.g., Frewitt, Fitzpatrick) | • Screen size<br>• Feeder speed<br>• Position of knives or hammers<br>• Mill speed | |
| Drying | Oven (e.g., Waldner, Introtherm, O'Hara, & Colton) | • Inlet air temperature<br>• Drying time<br>• Air Flow rate<br>• Humidity of inlet air<br>• Loading of trays (pattern and amount) | • Moisture content<br>• Particle size distribution (after milling) |
| | Fluid bed (e.g., Niro, Glatt) | • Inlet air temperature<br>• Humidity of inlet air<br>• Drying time<br>• Air Flow rate<br>• Filter bag pore size<br>• Plate mesh | |
| Tabletting | Force feed (e.g., Fette, Korsh, Manesty, Kikusui, Courtuoy, etc.), Centrifugal (IMA) | • Pre-compression and final Compression machine setting<br>• Tabletting speed<br>• Maximum/minimum compression force<br>• Speed of force feeder<br>• Punch design<br>• Holding time | • Content uniformity<br>• Assay<br>• Hardness<br>• Friability<br>• Disintegration<br>• Weight<br>• Weight variation<br>• Thickness<br>• Visual Inspection/Appearance<br>• Dissolution Point or Profile<br>• Microbial (if applicable) |
| Encapsulator | Pellet dosing chamber (e.g., Bosch GKF) | • Machine setting<br>• Encapsulator speed<br>• Holding time<br>• Dosator height | • Content uniformity<br>• Assay<br>• Disintegration<br>• Weight |

 

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| Process Step | Type (Examples) | Potential Critical Process Parameters | Potential Critical Quality Attributes |
|---|---|---|---|
| Printing | Printing machine (Ackley Printer & Sorter) | • Belt speed | • Visual Inspection<br>• Microbial (if applicable) |
| Metal Detection | Metal detection (e.g., Safeline, Yamato, etc.) | • Sensitivity<br>• Speed and slope angle | • Yield & reject quantity |
| Sorting | Check weighing (e.g., Bosch KKE, Mocon) | • Tolerances<br>• Sensitivity<br>• Speed | • Weight |
| | Dimensional (e.g., Proquip) | • Gap setting<br>• Speed | • Yield |
| | Vision systems (e.g., Ikegami) | • Speed<br>• Sensitivity (shape/color, stain, diameter, &chipping)<br>• Hopper material level<br>• Air pressure | • Yield |

 