

**Guidance Number: 44**

**Table 1: Typical potential critical process parameters**

<b>Process Step</b>	<b>Type (Examples)</b>	<b>Potential Critical Process Parameters</b>	<b>Potential Critical Quality Attributes</b>
Mixing/lubrication	Bin blender (e.g., Servolift, Galley, Matcon, Bohle)	<ul style="list-style-type: none"> <li>• Mixing time</li> <li>• Speed</li> <li>• Order of addition</li> <li>• Change in direction</li> <li>• Holding time (for final blend)</li> <li>• Load size</li> </ul>	<ul style="list-style-type: none"> <li>• Homogeneity, potency</li> <li>• Particle size distribution</li> <li>• Bulk density or Specific volume</li> <li>• Moisture (in case of Osmotic blend)</li> <li>• Compactability</li> <li>• Bulk Flowability</li> </ul>
	Planetary blender (e.g., Herbst, AMF, Hobart)	<ul style="list-style-type: none"> <li>• Mixing time</li> <li>• Speed</li> <li>• Impeller configuration</li> <li>• Order of addition</li> <li>• Change in direction</li> <li>• Holding time (for final blend)</li> <li>• Load size</li> </ul>	<ul style="list-style-type: none"> <li>• Static Charge</li> </ul>
	Tumble blenders (Double cone blender and PK-V-blender)	<ul style="list-style-type: none"> <li>• Mixing time</li> <li>• Speed</li> <li>• I-bar speed (if used)</li> <li>• Order of addition</li> <li>• Holding time (for final blend)</li> <li>• Load size</li> </ul>	
	High shear blender (e.g., Diosna, Collette Gral, Fielder Spectrum)	<ul style="list-style-type: none"> <li>• Impeller mixing time</li> <li>• Impeller Speed</li> <li>• Chopper mixing time and speed</li> <li>• Order of addition</li> <li>• Holding time (for final blend)</li> <li>• Load size</li> </ul>	
Granulation binder preparation	Stirring vessel for binder solution	<ul style="list-style-type: none"> <li>• Mixing time</li> <li>• Speed</li> <li>• Temperature</li> <li>• Holding time</li> </ul>	<ul style="list-style-type: none"> <li>• Homogeneity of solution (clear)</li> </ul>
Dry granulation	Roller compactor (e.g., Bepex & Frewitt, Fitzpatrick Chilsonator, Gerteis, & Vector)	<ul style="list-style-type: none"> <li>• Compression force</li> <li>• Roll speed</li> <li>• Roll force</li> <li>• Screen size and type</li> <li>• Feed rate</li> <li>• Type of roll used</li> <li>• Temperature</li> <li>• Roller gap width</li> <li>• Tamp to Feed (auger ratio)</li> </ul>	<ul style="list-style-type: none"> <li>• Moisture content</li> <li>• Bulk density</li> <li>• Particle size distribution</li> <li>• Ribbon solid fraction</li> <li>• Ribbon tensile strength</li> <li>• Compressibility</li> </ul>

Process Step	Type (Examples)	Potential Critical Process Parameters	Potential Critical Quality Attributes
Wet granulation	Planetary blender (e.g., Herbst & AMF)	<ul style="list-style-type: none"> <li>• Mixing time</li> <li>• Speed</li> <li>• Rate of liquid addition (time &amp; quantity)</li> <li>• Temperature</li> <li>• Application method</li> <li>• Quantity of binder solution</li> <li>• Load size</li> </ul>	<ul style="list-style-type: none"> <li>• Moisture content</li> <li>• Bulk density</li> <li>• Particle size distribution</li> <li>• Homogeneity (of the dry blend before granulation)</li> </ul>
	High shear blender (e.g., Diosna, Collette Gral, Fielder Spectrum)	<ul style="list-style-type: none"> <li>• Impeller configuration</li> <li>• Impeller speed</li> <li>• Chopper configuration</li> <li>• Chopper speed</li> <li>• Mixing time</li> <li>• Order of addition</li> <li>• Temperature</li> <li>• Application method</li> <li>• Quantity of binder solution</li> <li>• Load size</li> </ul>	
	Low shear blender and drier (e.g., PK V- blender Processor)	<ul style="list-style-type: none"> <li>• Blending speed</li> <li>• Blending time</li> <li>• I-bar setting (speed)</li> <li>• Rate of liquid addition (time &amp; quantity)</li> <li>• Quantity of binder addition</li> <li>• Temperature</li> <li>• Load size</li> </ul>	
Milling (wet or dry)	Oscillator (Frewitt)	<ul style="list-style-type: none"> <li>• RPM</li> <li>• Screen size</li> <li>• Pressure</li> <li>• Temperature</li> <li>• Holding time</li> <li>• Position of knives or hammers</li> <li>• Feeder speed</li> <li>• Impeller used</li> <li>• Gap for impeller</li> </ul>	<ul style="list-style-type: none"> <li>• Bulk density</li> <li>• Particle size distribution</li> <li>• De-agglomeration</li> </ul>

Process Step	Type (Examples)	Potential Critical Process Parameters	Potential Critical Quality Attributes
	Cone mill (e.g., Comill)	<ul style="list-style-type: none"> <li>• RPM</li> <li>• Screen size</li> <li>• Feeder speed</li> <li>• Impeller (blade) type</li> <li>• Gap for impeller</li> </ul>	
	Hammer mill (e.g., Frewitt, Fitzpatrick)	<ul style="list-style-type: none"> <li>• Screen size</li> <li>• Feeder speed</li> <li>• Position of knives or hammers</li> <li>• Mill speed</li> </ul>	
Drying	Oven (e.g., Waldner, Introtherm, O'Hara, & Colton)	<ul style="list-style-type: none"> <li>• Inlet air temperature</li> <li>• Drying time</li> <li>• Air Flow rate</li> <li>• Humidity of inlet air</li> <li>• Loading of trays (pattern and amount)</li> </ul>	<ul style="list-style-type: none"> <li>• Moisture content</li> <li>• Particle size distribution (after milling)</li> </ul>
	Fluid bed (e.g., Niro, Glatt)	<ul style="list-style-type: none"> <li>• Inlet air temperature</li> <li>• Humidity of inlet air</li> <li>• Drying time</li> <li>• Air Flow rate</li> <li>• Filter bag pore size</li> <li>• Plate mesh</li> </ul>	
Tabletting	Force feed (e.g., Fette, Korsh, Manesty, Kikusui, Courtuoy, etc.), Centrifugal (IMA)	<ul style="list-style-type: none"> <li>• Pre-compression and final Compression machine setting</li> <li>• Tabletting speed</li> <li>• Maximum/minimum compression force</li> <li>• Speed of force feeder</li> <li>• Punch design</li> <li>• Holding time</li> </ul>	<ul style="list-style-type: none"> <li>• Content uniformity</li> <li>• Assay</li> <li>• Hardness</li> <li>• Friability</li> <li>• Disintegration</li> <li>• Weight</li> <li>• Weight variation</li> <li>• Thickness</li> <li>• Visual Inspection/Appearance</li> <li>• Dissolution Point or Profile</li> <li>• Microbial (if applicable)</li> </ul>
Encapsulator	Pellet dosing chamber (e.g., Bosch GKF)	<ul style="list-style-type: none"> <li>• Machine setting</li> <li>• Encapsulator speed</li> <li>• Holding time</li> <li>• Dosator height</li> </ul>	<ul style="list-style-type: none"> <li>• Content uniformity</li> <li>• Assay</li> <li>• Disintegration</li> <li>• Weight</li> </ul>

Process Step	Type (Examples)	Potential Critical Process Parameters	Potential Critical Quality Attributes
	Dosing disc (e.g., Bosch GKF)	<ul style="list-style-type: none"> <li>Machine settings (vacuum, pressure, etc.)</li> <li>Encapsulator speed</li> <li>Dosing disc size</li> <li>Holding time</li> <li>Tamping pins and settings</li> </ul>	<ul style="list-style-type: none"> <li>Weight variation</li> <li>Visual inspection</li> <li>Dissolution</li> <li>Microbial (if applicable)</li> </ul>
	Dosator (e.g., MG2 G 120, Zanasi)	<ul style="list-style-type: none"> <li>Machine settings (powder bed height, vacuum pull, etc.)</li> <li>Encapsulator speed</li> <li>Holding time</li> <li>Dosator height</li> </ul>	
Laser drilling	Lumonics Laser Drill	<ul style="list-style-type: none"> <li>Pulse on time</li> <li>Hole position</li> <li>Eject delay</li> </ul>	<ul style="list-style-type: none"> <li>Orifice size</li> <li>Orifice location</li> <li>Visual inspection</li> </ul>
Film Coating	Perforated pan (e.g., Glatt, Vector, Accela-Cota)	<ul style="list-style-type: none"> <li>Coating pan settings</li> <li>Outlet air temperature</li> <li>Spray rate</li> <li>Spray air pressure/pattern</li> </ul>	<ul style="list-style-type: none"> <li>Visual inspection/Elegance</li> <li>Dissolution</li> <li>Moisture content</li> <li>Microbial (if applicable)</li> </ul>
Film Coating (continues)	Fluidized bed (e.g., Huttlin HKC)	<ul style="list-style-type: none"> <li>Nozzle size</li> <li>Gun angle</li> <li>Distance between guns</li> <li>Distance of the guns to the tablet bed</li> <li>RPM</li> <li>Quantity of suspension/solution</li> <li>Holding time</li> </ul>	
Coating solution/suspension preparation	Stirring vessel	<ul style="list-style-type: none"> <li>Mixing speed</li> <li>Mixing time</li> <li>Temperature</li> <li>Order of addition</li> <li>Holding time</li> </ul>	<ul style="list-style-type: none"> <li>Viscosity</li> <li>Specific gravity</li> <li>Microbial</li> <li>Homogeneity of suspension (free of agglomerates)</li> </ul>
Membrane Coating	Perforated pan (Vector Hi-Coater)	<ul style="list-style-type: none"> <li>Load size</li> <li>Gun to bed distance</li> <li>Inlet Air Flow</li> <li>Exhaust temperature</li> <li>Spray rate</li> <li>Pan speed</li> </ul>	<ul style="list-style-type: none"> <li>Coating weight gain</li> <li>Thickness</li> <li>Visual inspection</li> <li>Dissolution point or profile</li> <li>Moisture content</li> <li>Degradants</li> <li>Microbial (if applicable)</li> </ul>

Process Step	Type (Examples)	Potential Critical Process Parameters	Potential Critical Quality Attributes
Printing	Printing machine (Ackley Printer & Sorter)	<ul style="list-style-type: none"> <li>• Belt speed</li> </ul>	<ul style="list-style-type: none"> <li>• Visual Inspection</li> <li>• Microbial (if applicable)</li> </ul>
Metal Detection	Metal detection (e.g., Safeline, Yamato, etc.)	<ul style="list-style-type: none"> <li>• Sensitivity</li> <li>• Speed and slope angle</li> </ul>	<ul style="list-style-type: none"> <li>• Yield &amp; reject quantity</li> </ul>
Sorting	Check weighing (e.g., Bosch KKE, Mocon)	<ul style="list-style-type: none"> <li>• Tolerances</li> <li>• Sensitivity</li> <li>• Speed</li> </ul>	<ul style="list-style-type: none"> <li>• Weight</li> </ul>
	Dimensional (e.g., Proquip)	<ul style="list-style-type: none"> <li>• Gap setting</li> <li>• Speed</li> </ul>	<ul style="list-style-type: none"> <li>• Yield</li> </ul>
	Vision systems (e.g., Ikegami)	<ul style="list-style-type: none"> <li>• Speed</li> <li>• Sensitivity (shape/color, stain, diameter, &amp; chipping)</li> <li>• Hopper material level</li> <li>• Air pressure</li> </ul>	<ul style="list-style-type: none"> <li>• Yield</li> </ul>