

## **Guidance Number 036:**

**Table 1: Bottle Packaging –common potentially critical process parameters.**

<b>Process Step</b>	<b>Equipment Type (Examples)</b>	<b>Potential Critical Process Parameters<sup>a,b</sup></b>	<b>Potential Critical Quality Attributes<sup>a,b</sup></b>
Unscrambler Machine/Bottle blower	Blowers and vacuum (Omega, Bausch & Strobel, Farmomac, Kaps, Marchesini, IMA, King, Nova, New England)	<ul style="list-style-type: none"><li>• Speed</li><li>• Air pressure/velocity</li><li>• Vacuum</li></ul>	<ul style="list-style-type: none"><li>• Visual cleanliness (particulate free)</li></ul>
Desiccant Feeder	Omega Design	<ul style="list-style-type: none"><li>• Speed</li></ul>	<ul style="list-style-type: none"><li>• Quantity of desiccant(s) per bottle</li></ul>
Bottle Filler	Lakso, Merrill	<ul style="list-style-type: none"><li>• Slat size</li><li>• Speed</li><li>• Manifold</li></ul>	<ul style="list-style-type: none"><li>• Accuracy of count (short/over count)</li></ul>

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Process Step	Equipment Type (Examples)	Potential Critical Process Parameters <sup>a,b</sup>	Potential Critical Quality Attributes <sup>a,b</sup>
Counters (tablet, bottle, slat)	Vision (Swiftpack, Conta), King, Lasko_	<ul style="list-style-type: none"> <li>• Speed (bottles, tablets,)</li> <li>• Set up according to tablet or bottle size, shape weight</li> </ul>	<ul style="list-style-type: none"> <li>• Accuracy of count (error rate)</li> </ul>
Checkweigher	Hi Speed , Gravimetric, X-Ray (Garvens, Techno-Europa Ramsey, Bosch, Harro-Hofliger, Mettler-Toledo)	<ul style="list-style-type: none"> <li>• Capable of reading at the speed used</li> <li>• Sensitivity setting</li> <li>• Time to weigh (gravimetric)</li> <li>• Speed or rate</li> <li>• Vibration</li> </ul>	<ul style="list-style-type: none"> <li>• Accuracy</li> </ul>
Cottoning	Lakso, Fowler/Zalkin	<ul style="list-style-type: none"> <li>• Guillotine set up</li> <li>• Cottoner inserts length</li> <li>• Cotton length</li> </ul>	<ul style="list-style-type: none"> <li>• Visual Inspection cotton per bottle</li> <li>• No broken tablets</li> </ul>
Torque monitors (could be part of capper)	Accutek, Sure Torque, Equatorque, NJM/CLI Packaging,	<ul style="list-style-type: none"> <li>• Speed (cap and quill)</li> <li>• Height adjustment</li> <li>• Torque input and accuracy (no slippage during testing)</li> <li>• Ability to handle child-resistant and/or squeeze and turn caps.</li> <li>• Bottle or closure grips (size, design, and grip materials)</li> </ul>	<ul style="list-style-type: none"> <li>• Cap (cap or thread) damage rate</li> <li>• Reject rate</li> <li>• Statistical analysis (if applicable)</li> </ul>
Cappers	Lakso, Fowler, New England Machine, Resina, Kapsall	<ul style="list-style-type: none"> <li>• Speed</li> <li>• Grips</li> <li>• Set-up height</li> <li>• Top pressure (rotary capper)</li> <li>• Spindle speed (rotary capper)</li> </ul>	<ul style="list-style-type: none"> <li>• Removal torque</li> <li>• High Cap</li> <li>• Missing Cap (presence)</li> <li>• Skew</li> </ul>
Induction Sealer	Enercon	<ul style="list-style-type: none"> <li>• Sealing temperature</li> <li>• Speed</li> </ul>	<ul style="list-style-type: none"> <li>• Visual Inspection of seal integrity</li> </ul>
Cap Retorquer	New England, Newmann	<ul style="list-style-type: none"> <li>• Speed</li> </ul>	<ul style="list-style-type: none"> <li>• Removal torque</li> </ul>
Tamper Evident Equipment	Over wrapper Neck banders	<ul style="list-style-type: none"> <li>• Material indexing</li> <li>• Speed</li> </ul>	<ul style="list-style-type: none"> <li>• Visual Inspection</li> </ul>
Reject verification	Automation based (shift registration, reject control, reject confirmation)	<ul style="list-style-type: none"> <li>• Rate</li> </ul>	<ul style="list-style-type: none"> <li>• Visual Inspection- rejection.</li> </ul>
Labeler Machine	Krones, Accraply, Pressure-sensitive, Thermo-Sensitive, Shrink, Mylar, etc. (Pago, ESF, CVC)	<ul style="list-style-type: none"> <li>• Rate</li> <li>• Glue temperature (if applicable, for outserts)</li> <li>• Pressure (if applicable)</li> </ul>	<ul style="list-style-type: none"> <li>• Visual inspection- label</li> <li>• Label/outsert position</li> <li>• Quality and position of printed lot number and expiration date</li> </ul>
Labeler/Outserter	Weiler		
Outserter Machine	Hoppman, Com-tal		

Process Step	Equipment Type (Examples)	Potential Critical Process Parameters <sup>a,b</sup>	Potential Critical Quality Attributes <sup>a,b</sup>
Printers	Hot foil, embossing, debossing, flexographic, stamp/pad, laser digital, ink jet, thermal	<ul style="list-style-type: none"> <li>Speed</li> </ul>	<ul style="list-style-type: none"> <li>Print quality (accuracy and legibility)</li> </ul>
Leaflet Folders/Inserters	MGS Machine, IMA, GUK	<ul style="list-style-type: none"> <li>Glue temperature (if applicable)</li> <li>Speed</li> </ul>	<ul style="list-style-type: none"> <li>Visual inspection- leaflet</li> <li>Position</li> </ul>
Bundling/shrinking/Overwrapper	Pester, Tevopharm	<ul style="list-style-type: none"> <li>Speed (rate)</li> <li>Temperature</li> </ul>	<ul style="list-style-type: none"> <li>Bundles appearance</li> <li>Number of bottles per bundle</li> </ul>
Casepacker Machine	Skinetta, Schubert	<ul style="list-style-type: none"> <li>Speed and accuracy</li> </ul>	<ul style="list-style-type: none"> <li>Number of package per case</li> <li>Low fill</li> </ul>
Cartoner	Bosch- Contina, Bedo, Jones, ADCO	<ul style="list-style-type: none"> <li>Depth and legibility of the emboss/ deboss</li> <li>Feed mechanism and rate</li> </ul>	<ul style="list-style-type: none"> <li>Visual inspection- debossing</li> <li>Units per carton</li> </ul>
Bar Coders	Laetus, Kaps, Sartorius	<ul style="list-style-type: none"> <li>Speed</li> </ul>	<ul style="list-style-type: none"> <li>Visual inspection- bar code</li> <li>Readability</li> </ul>

<sup>a</sup> Potential CPPs and CQAs for filling and sealing steps are also covered in Semi-Solid Dosage Forms

<sup>b</sup> Environmental conditions (e.g. temperature, humidity, air cleanliness) may be common to any package operation where product or sensitive materials are exposed to the environment. Change parts and set-up are potentially critical for many operations, but not viewed as “process parameters”. Likewise drug product characteristics such as tablet durability and friability may also be common to any package operation where product handling becomes a potential critical property.

**Table 2- Blister Packaging – common critical process parameters.**

Process Step	Equipment Type (Examples)	Potential Critical Process Parameters <sup>a,b</sup>	Potential Critical Quality Attributes
Thermoformer	Körber Medipak, Uhlmann, Bosch-Servac, Marchesini)	<ul style="list-style-type: none"> <li>Sealing temperatures (lower, upper, cooling)</li> <li>Heater plate temperature</li> <li>Dwell time</li> <li>Cycle rate/timing cycle</li> <li>Forming pressure</li> <li>Filling speed</li> <li>Blister material characteristics</li> <li>Quality of tooling</li> <li>Print register (for pre-pre-printed foils)</li> <li>Camera function-at filling speed and rate</li> </ul>	<ul style="list-style-type: none"> <li>Leakage rates</li> <li>Appearance (e.g. visual inspection, legibility)</li> <li>Dimensional analysis (including thickness)</li> <li>Automated inspection (including product control camera)</li> <li>Security system challenges</li> <li>Foil registration</li> <li>Seal strength</li> <li>Moisture vapor transmission rates (during development)</li> </ul>
Feeder	Aylward	<ul style="list-style-type: none"> <li>Air pressures (frame and pins)</li> <li>Feed rate</li> </ul>	<ul style="list-style-type: none"> <li>Potential damage rate</li> <li>Number of dosage form per blister</li> </ul>

Process Step	Equipment Type (Examples)	Potential Critical Process Parameters <sup>a,b</sup>	Potential Critical Quality Attributes
Printer	Medtronic	<ul style="list-style-type: none"> <li>• Speed</li> </ul>	<ul style="list-style-type: none"> <li>• Readability of the printed information</li> </ul>
Cartoner	Uhlmann, Bosch-Contina, Bedo, Jones, ADCO	<ul style="list-style-type: none"> <li>• Feed mechanism and speed</li> <li>• Glue temperature (if applicable)</li> <li>• Coding station</li> </ul>	<ul style="list-style-type: none"> <li>• Visual inspection of carton for damage</li> <li>• Units per carton</li> <li>• Legibility of code</li> </ul>
Checkweigher	Yamato, Mettler Toledo	<ul style="list-style-type: none"> <li>• Capable of reading at the speed used</li> <li>• Sensitivity setting</li> <li>• Time to weigh (gravimetric)</li> <li>• Speed or rate</li> <li>• Temperature (if affecting weighing mechanism)</li> <li>• Vibration</li> </ul>	<ul style="list-style-type: none"> <li>• Accuracy</li> </ul>
Case Packer	Pester,	None	<ul style="list-style-type: none"> <li>• Number of package per case</li> </ul>
Bar Coders (see Table 1)			
Print & Apply	Multisystems	None	<ul style="list-style-type: none"> <li>• Readability of the printed information</li> </ul>

<sup>a</sup> Potential CPPs for filling and sealing steps are also covered in Semi-Solid Dosage Forms CPPs

<sup>b</sup> Environmental conditions (e.g. temperature, humidity, air cleanliness) may be common to any package operation where product or sensitive materials are exposed to the environment. Change parts and set-up are potentially critical for many operations, but not viewed as “process parameters”. Product specific evaluation is important. Likewise drug product characteristics such as tablet durability and friability may also be common to any package operation where product handling becomes a potential critical property.

**Table 3- Other Packaging Steps –common critical process parameters**

Process Step	Equipment Type (Examples)	Potential Critical Process Parameters	Potential Critical Quality Attributes
Blow-Fill- Seal	Nikka Densok rommeLag, Marchesini	<ul style="list-style-type: none"> <li>• See blister filling/sealing</li> <li>• Sealing temperatures (uniformity)</li> <li>• Heater plate, chilled water temperatures</li> <li>• Timing cycle</li> <li>• Forming pressures and seal pressure uniformity</li> <li>• Chiller differentials</li> <li>• Seal dwell time</li> <li>• Filling speed</li> <li>• Quality of tooling, seal gaskets</li> </ul>	<ul style="list-style-type: none"> <li>• See blisters</li> <li>• Leak test (package integrity)</li> <li>• Visual Inspection (forming/sealing defects)</li> <li>• Statistical weight checks</li> <li>• Dimensional Analysis (e.g. thickness)</li> <li>• Registration</li> <li>• Seal strength</li> </ul>

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<b>Process Step</b>	<b>Equipment Type (Examples)</b>	<b>Potential Critical Process Parameters</b>	<b>Potential Critical Quality Attributes</b>
Crimpers	Cozzoli, Optijma, flexicon	<ul style="list-style-type: none"> <li>• Jaw pressure</li> <li>• Height settings</li> <li>• Temperature (if applicable)</li> </ul>	<ul style="list-style-type: none"> <li>• Crimp dimensions (e.g. height)</li> <li>• Leakage rates</li> </ul>
Product Transfer Systems	Drum inverters Powder transfers (vacuum, air transfer)	<ul style="list-style-type: none"> <li>• Vacuum/air setting</li> </ul>	<ul style="list-style-type: none"> <li>• Impact on product integrity (e.g. friability, powder particle size distribution, powder segregation)</li> </ul>
Palletizer	Uhlman, Pasco, FKI Logistex	None	None