Steps using packaging equipment should be evaluated to determine which steps or pieces of equipment are considered critical. Examples of potential critical packaging steps/equipment systems may include:

- Reject systems (e.g. vision systems, weighing systems)
- Product and/or lot specific labeling systems
- Bottle and blister filling equipment
- Filling and capping equipment
- Induction seal units
- Tamper resistant packaging equipment
- Tablet and capsule feeding equipment
- Lot and bar coding equipment (both printing and reading of bar codes)
- Desiccant or other material feeders
- Bottle cleaning equipment (e.g. blowers and vacuums)
- Re-torque equipment
- Outserters and Inserters
- Other related to packaging (storage tanks prior to packaging, blow-fill-seal machines)

Equipment is subject to routine maintenance, calibration, challenges, etc. to ensure it is properly functioning. These practices should be taken into account when determining the criticality.

Potential CPPs and CQAs for these equipment and systems were addressed for some common packaging processes for solid dosage forms in Tables 1-3. Depending on the specific dosage form, product or packaging, some of the attributes listed below may not be applicable or additional attributes could be warranted. The following tables can be used as a starting point for the selection of CPPs and CQAs for an assessment of packaging validation requirements.

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

Process Step	Equipment Type (Examples)	Potential Critical Process Parameters[a,b]	Potential Critical Quality Attributes[a,b]
Unscrambler Machine/Bottle blower	Blowers and vacuum (Omega, Bausch & Strobel, Farmomac, Kaps, Marchesini, IMA, King, Nova, New England)	• Speed • Air pressure/velocity • Vacuum	• Visual cleanliness (particulate free)
Desiccant Feeder	Omega Design	• Speed	• Quantity of desiccant(s) per bottle
Bottle Filler	Lakso, Merrill	• Slat size • Speed • Manifold	• Accuracy of count (short/over count)

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

[a] Potential CPPs for filling and sealing steps are also covered in Semi-Solid Dosage Forms CPPs

[b] 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	• See blister filling/sealing • Sealing temperatures (uniformity) • Heater plate, chilled water temperatures • Timing cycle • Forming pressures and seal pressure uniformity • Chiller differentials • Seal dwell time • Filling speed • Quality of tooling, seal gaskets	• See blisters • Leak test (package integrity) • Visual Inspection (forming/sealing defects) • Statistical weight checks • Dimensional Analysis (e.g. thickness) • Registration • Seal strength

- Discussion of the data compared to their respective acceptance criteria;
- Review of critical process parameters from lot packaging records;
- Description of any deviations or failures, and their impact on the validation; and
- Conclusions.

Matrixing and Bracketing
Matrixing of the packaging processes can be performed when there are significant similarities between products. The rationale for matrixing must be included in the protocol.

Example:
A solid dosage form is compounded in various strengths affecting its overall shape and size. Solid dosage units are packaged with the same tools in the same type of container/closure. One validation run for each tablet strength should be included in the validation matrix.

Bracketing of the packaging processes can be performed when there is a range of process extremes of parameters. Different products may be bracketed due to similarities of package components, critical packaging process parameters, packaging lines, and product attributes.

The rationale for the bracketing approach should be included in the protocol.

Example:
In the case where bottle dimensions for different products are identical except for height and only a minor line adjustment is required.

Example:
Largest and smallest filling amounts, fastest and slowest operating speeds for the packaging process

Number of Validation Runs (or segments)
A packaging validation run should be representative of the typical packaging process and be of sufficient length such that the packaging validation run will exhibit normal packaging process variability such as equipment variability, operator and mechanic variability, material variability, start-ups, shut downs, shift changes, and environmental conditions. Some sites use a minimum run time such as 10 hours to capture any potential effects of a shift change.

However, within a continuous quality verification (CQV) approach, CQAs and/or CPPs may be continuously monitored, evaluated and adjusted (directly or indirectly via critical process parameters). In this approach, the number of packaging validation runs or segments is not applicable. Techniques such as control charting and trending may be performed in an at-line or on-line manner. This approach conforms to the Continued Process Verification (Stage 3) and controls, as described in the FDA's new draft guidance on process validation.

