Status

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Guidance Elements

- Selected guidance documents relying on research publications
  - Solid state chemical attributes
  - Performance attributes
  - Principles of operation
  - Toxicity
- Part of the overall strategy
  - Quality metrics
  - Standards

Co-Crystals

- Regulatory Classification of Pharmaceutical Co-Crystals
  - Final Guidance, April, 2013
  - **Co-crystals:** Crystalline materials composed of two or more molecules within the same crystal lattice.
  - Can be regarded as “co-crystal drug product intermediate”

Co-Crystals

- API and its excipient(s) have a ΔpKa (pKa (base) - pKa (acid)) < 1
  - active ingredient-excipient complex is a "co-crystal drug product intermediate"
- Otherwise: Spectroscopic tools are needed to demonstrate the same
- Need not consider these as new API

Tablet Scores to Facilitate Tablet Splitting

- Tablet Scoring: Nomenclature, Labeling and Data for Evaluation
  - Final Guidance, March, 2013
  - **Tablet Scores:** Guidelines to follow, data to provide, and criteria to meet and detail in an application to support approval of a scored tablet

Tablet Scores

- Concerns with splitting a tablet include:
  - Variations in the tablet content, Weight, Disintegration, or Dissolution and Stability
- The split tablet portions should meet the same finished-product testing requirements as for a whole-tablet product with equivalent strength
- Should not be below the minimum therapeutic dose

Size of Beads for Sprinkle Product

- Size of Beads in Drug Products Labeled for Sprinkle
  - Final Guidance, May, 2012
  - **Sprinkle Product:** it is important to have reasonable assurance that the patient will be able to swallow the beads (uncrushed) with the food with which the beads are mixed without stimulating the urge to chew

Sprinkle

- Target bead size up to 2.5 mm with no more than 10 percent variation over this size, to a Maximum size of 2.8 mm
- May propose a target and maximum bead size equal to or less than that used in the currently approved RLD
- Enteral feeding
  - all of the beads (uncrushed) be able to safely pass through the feeding tube and not cause tube occlusions

SUPAC Equipment

- SUPAC: Manufacturing Equipment Addendum
  - Draft Guidance, April, 2013
  - **Combined Manufacturing Equipment Addendum for SUPAC IR and SUPAC MR:** Intended to help the manufacturer determine the documentation regarding manufacturing equipment changes

SUPAC

- Removes list of equipment models
- Moves toward operating principles and design characteristics for broad categories of unit operation
  - Particle size reduction and/or separation, mixing, emulsification, deaeration, transfer, and packaging
  - Follow a risk-based approach that includes a rationale
  - Address the impact on the product quality attributes of equipment variations

Phthalates as Excipients

- Limiting the Use of Certain Phthalates as Excipients in CDER-Regulated Products
  - Final Guidance, December, 2012
  - **DBP and DEHP:** Manufacturers with products that contain DBP or DEHP should consider alternative excipients
  - dibutyl phthalate (DBP)
  - di(2-ethylhexyl) phthalate (DEHP)

Phthalates

- Does **NOT** address DBP or DEHP content due to the presence of an impurity—including as a result of leaching from packaging materials and delivery systems
- Follows actions by CPSC, European Commission, EPA and CDRH
- The Agency generally does not consider DBP or DEHP safe or suitable as an inactive ingredient in OTC monograph products

Federal Register

- FR vol. 76, No. 245; Gluten in Drug Products
  - FDA-2011-N-0842
  - Request for Information and comments
  - How prevalent is the use of wheat product?
  - Is there a test methodology in use?
  - What would be impact of not using wheat product?

Active Older Documents

- Annual Reportable Changes Guidance
  - Draft Guidance; 2010
- Comparability Protocols
  - Draft Guidance; 2003
- Liposome Products
  - Draft Guidance; 2002
- Metered Dose Inhaler and Dry Powder Inhaler
  - Draft Guidance; 1998


2012

End

Say what you do

Do what you say