Combination Products/New Technologies/Difficult to Compound Products

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What is a combination product?

- Recognized in the FD&C Act and defined in regulations (21 CFR 3.2(e)), in part as:
  - (1) A product comprised of two or more regulated components, i.e., drug/device, biologic/device, drug/biologic, or drug/device/biologic, that are physically, chemically, or otherwise combined or mixed and produced as a single entity
- Examples:
  - Monoclonal antibody combined with a therapeutic drug
  - Device coated or impregnated with a drug or biologic
    - Drug-eluting stent
    - Orthopedic implant with growth factors
  - Insulin injector pens
- Multiple center involvement where the Agency assigns a primary center that may consult or collaborate with another center as part of the review process

Combination products that you might observe being prepared in pharmacies

- Examples include:
  - Prefilled syringes
  - Metered dose Inhalers
  - Dry powder inhalers
  - Transdermal systems
  - Prefilled auto-injectors (e.g., EpiPen)
- Certain combination products can be complex
- To be better informed about combination products in the compounding context, request that states send any information (e.g., complaints, adverse events) to FDA regarding such products

What automated technologies are being used in compounding?

- Examples of technologies:
  - Incorporation of robotics
  - Blow-Fill-Seal systems used for unit dose production
  - Total parenteral nutrition devices

Adoption of New Technology

- In general, conventional manufacturers would undertake qualification and validation of such equipment, which includes:
  - DQ – design qualification
  - IQ – installation qualification
  - OP – operational qualification
  - PQ – performance qualification
- Helps to ensure the equipment is suitable for its intended purpose
- These checks are also important to compounders that might adopt such technology

Difficult to Compound List

- Drug products or categories of drug products identified on a list-by FDA by regulation as drug products or categories of drug products that present demonstrable difficulties for compounding do not qualify for the exemptions under sections 503A or 503B
- Generally, FDA has considered six criteria when evaluating whether a drug product or category of drug products is demonstrably difficult to compound:
  - (1) The complexity of the formulation;
  - (2) the complexity of the drug delivery mechanism;
  - (3) the complexity of the dosage form;
  - (4) the complexity of characterizing or controlling bioavailability;
  - (5) the complexity of the compounding process; and
  - (6) the complexity of physicochemical or analytical testing
- No regulations published yet

Difficult to Compound List

- DTC list is being developed in consultation with the Pharmacy Compounding Advisory Committee (PCAC)
- Identification of drug products that are difficult to compound by states will be helpful as the list is being developed
  - E.g., Controlled or extended release oral dosage forms

Thank you