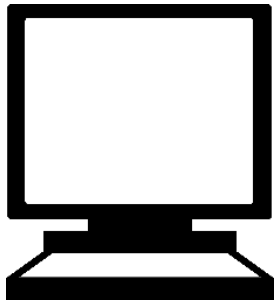
U.S. FOOD & DRUG ADMINISTRATION

Drug-Device Combination Products Quality Assessment

Ashley B. Boam, MSBE
Director
Office of Policy for Pharmaceutical Quality
CDER/OPQ

Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.



Pharmaceutical Quality

A quality product of any kind consistently meets the expectations of the user.

Drugs are no different.


Patients expect safe and effective medicine with every dose they take.

Pharmaceutical quality is

assuring *every* dose is safe and effective, free of contamination and defects.

It is what gives patients confidence in their *next* dose of medicine.

CDER-led Combination Products

Quality assessment includes:

- OPQ
  - CMC assessment (drug product, drug substance, manufacturing assessment)
- Consults to CDRH may be requested for:
  - Engineering/device design
    - Determined by drug product assessor (OLDP)
  - Manufacturing facilities and Quality System (21 CFR 820) Review
    - Determined by manufacturing assessor (OPMA)

Intercenter Consult Requests (ICCRs)

- Processes and expectations outlined in Staff Manual Guide (SMG) 4101, issued June 11, 2018
  - Timely issuance of consult requests between Centers
  - Content of consult requests
  - Expectations that consults will be completed in a manner to facilitate meeting relevant user fee goals
  - Procedures for informal and formal dispute resolution
- Reviewer guides available on when to request an ICCR and who to contact if unsure

ICCRs for Engineering/Device Design

- CDRH assessment typically addresses:
  - Device performance (at release and throughout shelf-life)
  - Biocompatibility of patient-contacting materials not in contact with the drug
  - Control strategy for key device attributes
- Note that OPQ assessment addresses:
  - Compatibility of drug and device components
  - Sterility (as provided by the primary container closure)

CGMPs for Combination Products

- Requirements outlined in 21 CFR part 4 and Guidance for Industry *Current Good Manufacturing Practice Requirements for Combination Products*, January 2017
- Drug-device combination products are subject to the CGMP requirements applicable to each constituent part, which include drug CGMP regulations (21 CFR parts 210 and 211) and the device Quality System (QS) regulation (21 CFR part 820)
- Demonstration of compliance with the drug CGMP and device QS regulation requirements may include a streamlined approach, and there may be combination products that are exempt from device QS regulation requirements because of exemptions applicable to their device constituent parts
- *Streamlined approach (21 CFR 4.4(b))*. Co-packaged and single-entity combination products manufacturers that are subject to both the drug CGMPs and device QS regulation may:
  - Implement either the drug CGMPs (210 and 211) or device quality system regulation (820) rather than both,
  - IF they also implement specified provisions of the other of these two sets of CGMP requirements

Specified Provisions from 21 CFR 820

Provisions to be added under the *streamlined approach* when the drug CGMPs are implemented:

- 21 CFR 820.20 – Management responsibility
- 21 CFR 820.30 – Design controls
- 21 CFR 820.50 – Purchasing controls
- 21 CFR 820.100 – Corrective and preventive action
- 21 CFR 820.170 – Installation (as applicable)
- 21 CFR 820.200 – Servicing (as applicable)

ICCRs for Manufacturing Facilities and Quality System Review

- CDER-led combination products may have a facility assessment by both CDER/OPQ/OPMA and CDRH's Office of Product Evaluation and Quality (OPEQ) to ensure compliance with 21 CFR part 4, including:
  - Compliance with the 820 provisions
  - Whether a facility inspection is needed for facilities involved in the manufacture of the device constituent or the combination product
- Agreements reached between CDER and CDRH on when ICCRs are needed, generally based on product risk profile and facility compliance history
- ICCRs for facilities and QS review are independent of whether an ICCR is issued for engineering/product design
- Where preapproval inspections are conducted, an ICCR will generally be sent to CDRH when the EIR contains observations related to 21 CFR 820 requirements

Recommendations

- Provide testing on products using the final version of the device constituent part
- For single entity products, assess stability using the fully assembled, finished product
- Consult available guidance documents:
  - Guidance for Industry and FDA Staff *Technical Considerations for Pen, Jet, and Related Injectors Intended for Use with Drugs and Biological Products*
  - Guidance for Industry *Current Good Manufacturing Practice Requirements for Combination Products*
- Seek product-specific advice through Controlled Correspondence or pre-ANDA meetings (where applicable)

Thank you!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