Current Good Manufacturing Practices for Combination Products Final Rule

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Overview

- Thanks
- Background
- The rule
- Response to comments
- Next steps
- Take away
- Resources

Thanks

Working group on CGMPs for combination products:

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Background

- Combination products: Products comprised of a two or more types of medical products (biologic, device, and/or drug, not food or cosmetics . . .)

- Three kinds:
  - "Single-entity" (e.g., drug-eluting stent)
  - "Co-package" (e.g., first-aid or surgical kit, or a syringe packaged with vial of a drug)
  - "Cross-labeled" (e.g., certain light-emitting devices and light-activated drugs)

- Biological products also meet the definition of a drug or device, and human cellular and tissue-based products (HCT/Ps) may be constituent parts of combination products and regulated as drugs, devices, or biological products.

- Combination product manufacturers must comply with the CGMP requirements applicable to the biologics, devices, drugs, and HCT/Ps included in their combination products.

The Rule

- Existing CGMP regulations established minimum requirements to assure the safety, identity, strength, quality and purity, as applicable, of drugs, devices, biological products, and HCT/Ps.

- This rule addresses how to satisfy these CGMP requirements for combination products in a manner that ensures manufacture of a safe and effective product while avoiding redundant regulatory requirements.

Rule cont'd

- *Cross-labeled combination products*: Constituent parts are subject to the CGMP requirements applicable to that type of article (e.g., drug cGMPs if article is a drug).

- *Co-packaged and single-entity combination products*: Rule provides streamlined approach to comply with CGMP requirements.

Rule cont'd

- *Streamlined approach*. 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 (at 21 CFR 210 and 211) or device quality system regulation (at 21 CFR 820) rather than both,
  - IF they also implement specified provisions of the other of these two sets of CGMP requirements.
- The CGMPs for biological products under parts 600 through 680 and for HCT/Ps under part 1271 also must be met if applicable.

Specified requirements from QS regulation

- 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
- 21 CFR 820.200 - Servicing

Specified Requirements from drug CGMPs

- 21 CFR 211.84 - Testing and approval or rejection of components, drug product containers, and closures.
- 21 CFR 211.103 - Calculation of yield
- 21 CFR 211.132 - Tamper-evident packaging for over-the-counter (OTC) human drug products
- 21 CFR 211.137 - Expiration dating
- 21 CFR 211.165 - Testing and release for distribution
- 21 CFR 211.166 - Stability testing
- 21 CFR 211.167 - Special testing requirements
- 21 CFR 211.170 - Reserve samples

Response to comments

Frequently raised issues addressed by the rule include . . .

Scope of CGMP requirements

Q: Does the rule create any new CGMP requirements?

A: No, this rule merely clarifies how to comply with existing CGMP requirements and offers a mechanism to streamline compliance.

Q: Do facilities that are not otherwise subject to CGMPs become subject to them because of this rule?

A: No, this rule does not change to whom CGMP requirements apply.

Response to comments cont'd

"Device" v. "container closure system"

Q: Should delivery devices be treated as mere container closures or as prefilled devices?

A: Prefilled devices, so all manufacturing considerations can be appropriately addressed.

Design controls

Q: Do design controls apply to the combination product or just device constituent part(s)?

A: The combination product, to ensure appropriate selection of the constituent parts and appropriate evaluation of their interactions and interrelationships.

Product testing

Q: Can the product testing and release requirements called out from the drug CGMPs be applicable throughout the manufacturing process for the combination product?

A: Yes, as appropriate to confirm the product meets its specifications and performs properly.

Response to comments cont'd

Reserve samples

Q: Do reserve samples need to be kept of the combination product or only the drug constituent part?

A: Reserve samples should include the drug constituent part and the device constituent part/portion(s) of it that come into direct contact with the drug.

Biological product and HCT/P CGMP requirements

Q: Why doesn't the rule offer a similar streamlining option for biological product and HCT/P CGMPs?

A: These CGMPs address distinct issues. Biological CGMPs augment other CGMPs to address biological product issues, and current good tissue practice requirements address communicable disease risk.

Next Steps

- FDA completing draft companion guidance.
- Feedback welcome.
- Contact product coordinators, ORA, OCP as needed for your product/facility.

Take away

- Regulation of combination products
- Agency approach
- Working with FDA
- Looking forward and around

Resources

Rule available at (link also posted on OCP's webpage):

- https://www.federalregister.gov/articles/2013/01/22/2013-01068/current-good-manufacturing-practice-requirements-for-combination-products

CGMP guidance for medical products:

- http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm
- http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm
- http://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/default.htm

Resources cont'd

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