

of the single mode of action that provides the most important therapeutic action of the product, and the basis for that determination.

- (x) Schedule and duration of use;
- (xi) Dose and route of administration of drug or biologic;
- (xii) Description of related products, including the regulatory status of those related products; and
- (xiii) Any other relevant information.

(3) The sponsor's recommendation as to which agency component should have primary jurisdiction based on the mode of action that provides the most important therapeutic action of the combination product. If the sponsor cannot determine with reasonable certainty which mode of action provides the most important therapeutic action of the combination product, the sponsor's recommendation must be based on the assignment algorithm set forth in § 3.4(b) and an assessment of the assignment of other combination products the sponsor wishes FDA to consider during the assignment of its combination product.

(d) Where to file: all communications pursuant to this subpart shall be addressed to the attention of the product jurisdiction officer. Such a request, in its mailing cover should be plainly marked "Request for Designation." Concurrent submissions of electronic copies of Requests for Designation may be addressed to *combination@fda.gov*.

[56 FR 58756, Nov. 21, 1991, as amended at 68 FR 37077, June 23, 2003; 70 FR 49861, Aug. 25, 2005]

### § 3.8 Letter of designation.

(a) Each request for designation will be reviewed for completeness within 5 working days of receipt. Any request for designation determined to be incomplete will be returned to the applicant with a request for the missing information. The sponsor of an accepted request for designation will be notified of the filing date.

(b) Within 60 days of the filing date of a request for designation, the product jurisdiction officer will issue a letter of designation to the sponsor, with copies to the centers, specifying the agency component designated to have primary jurisdiction for the premarket review

and regulation of the product at issue, and any consulting agency components. The product jurisdiction officer may request a meeting with the sponsor during the review period to discuss the request for designation. If the product jurisdiction officer has not issued a letter of designation within 60 days of the filing date of a request for designation, the sponsor's recommendation of the center with primary jurisdiction, in accordance with § 3.7(c)(3), shall become the designated agency component.

(c) Request for reconsideration by sponsor: If the sponsor disagrees with the designation, it may request the product jurisdiction officer to reconsider the decision by filing, within 15 days of receipt of the letter of designation, a written request for reconsideration not exceeding 5 pages. No new information may be included in a request for reconsideration. The product jurisdiction officer shall review and act on the request in writing within 15 days of its receipt.

### § 3.9 Effect of letter of designation.

(a) The letter of designation constitutes an agency determination that is subject to change only as provided in paragraph (b) of this section.

(b) The product jurisdiction officer may change the designated agency component with the written consent of the sponsor, or without its consent to protect the public health or for other compelling reasons. A sponsor shall be given 30 days written notice of any proposed nonconsensual change in designated agency component. The sponsor may request an additional 30 days to submit written objections, not to exceed 15 pages, to the proposed change, and shall be granted, upon request, a timely meeting with the product jurisdiction officer and appropriate center officials. Within 30 days of receipt of the sponsor's written objections, the product jurisdiction officer shall issue to the sponsor, with copies to appropriate center officials, a written determination setting forth a statement of reasons for the proposed change in designated agency component. A non-consensual change in the designated

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agency component requires the concurrence of the Principal Associate Commissioner.

[56 FR 58756, Nov. 21, 1991, as amended at 68 FR 37077, June 23, 2003]

#### § 3.10 Stay of review time.

Any filing with or review by the product jurisdiction officer stays the review clock or other established time periods for agency action for an application for marketing approval or required investigational notice during the pendency of the review by the product jurisdiction officer.

### Subpart B [Reserved]

## PART 4—REGULATION OF COMBINATION PRODUCTS

### Subpart A—Current Good Manufacturing Practice Requirements for Combination Products

Sec.

- 4.1 What is the scope of this subpart?
- 4.2 How does FDA define key terms and phrases in this subpart?
- 4.3 What current good manufacturing practice requirements apply to my combination product?
- 4.4 How can I comply with these current good manufacturing practice requirements for a co-packaged or single-entity combination product?

### Subpart B [Reserved]

AUTHORITY: 21 U.S.C. 321, 331, 351, 352, 353, 355, 360, 360b–360f, 360h–360j, 360l, 360hh–360ss, 360aaa–360bbb, 371(a), 372–374, 379e, 381, 383, 394; 42 U.S.C. 216, 262, 263a, 264, 271.

SOURCE: 78 FR 4321, Jan. 22, 2013, unless otherwise noted.

### Subpart A—Current Good Manufacturing Practice Requirements for Combination Products

#### § 4.1 What is the scope of this subpart?

This subpart applies to combination products. It establishes which current good manufacturing practice requirements apply to these products. This subpart clarifies the application of current good manufacturing practice regulations to combination products, and

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provides a regulatory framework for designing and implementing the current good manufacturing practice operating system at facilities that manufacture co-packaged or single-entity combination products.

#### § 4.2 How does FDA define key terms and phrases in this subpart?

The terms listed in this section have the following meanings for purposes of this subpart:

*Biological product* has the meaning set forth in § 3.2(d) of this chapter. A biological product also meets the definitions of either a drug or device as these terms are defined under this section.

*Combination product* has the meaning set forth in § 3.2(e) of this chapter.

*Constituent part* is a drug, device, or biological product that is part of a combination product.

*Co-packaged combination product* has the meaning set forth in § 3.2(e)(2) of this chapter.

*Current good manufacturing practice operating system* means the operating system within an establishment that is designed and implemented to address and meet the current good manufacturing practice requirements for a combination product.

*Current good manufacturing practice requirements* means the requirements set forth under § 4.3(a) through (d).

*Device* has the meaning set forth in § 3.2(f) of this chapter. A device that is a constituent part of a combination product is considered a finished device within the meaning of the QS regulation.

*Drug* has the meaning set forth in § 3.2(g) of this chapter. A drug that is a constituent part of a combination product is considered a drug product within the meaning of the drug CGMPs.

*Drug CGMPs* refers to the current good manufacturing practice regulations set forth in parts 210 and 211 of this chapter.

*HCT/Ps* refers to human cell, tissue, and cellular and tissue-based products, as defined in § 1271.3(d) of this chapter. An HCT/P that is not solely regulated under section 361 of the Public Health Service Act may be a constituent part of a combination product. Such an HCT/P is subject to part 1271 of this