

FDA STAFF MANUAL GUIDES, VOLUME IV - AGENCY PROGRAM DIRECTIVES

COMBINATION PRODUCTS

EXPECTATIONS AND PROCEDURES FOR ENGAGEMENT AMONG MEDICAL PRODUCT CENTERS AND OFFICE OF COMBINATION PRODUCTS ON REGULATIONS AND GUIDANCE PERTAINING TO COMBINATION PRODUCTS

Effective Date: March 27, 2018

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**1. PURPOSE.**

The purpose of this staff manual guide is to ensure the necessary subject matter experts and policy staff from the medical product Centers (Center for Biologics Evaluation and Research (CBER), Center for Drug Evaluation and Research (CDER), Center for Devices and Radiological Health (CDRH)), and the Office of Combination Products (OCP) are engaged in a timely manner as needed for development and clearance of regulations and guidance documents that pertain to combination products<sup>1</sup> and that this engagement is transparent to stakeholders.<sup>2</sup>

**2. DEFINITIONS.**

**Component:** CDER, CBER, CDRH or OCP

**Lead Component:** The Component that has the lead for developing the guidance or regulation

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<sup>1</sup> See 21 CFR 3.2(e).

<sup>2</sup> Engagement of other FDA components (including other Centers, Office of Medical Products and Tobacco, Office of Chief Counsel and Office of Regulatory Affairs) may also be appropriate; however, when to engage such components is beyond the scope of this guide.

**Consulting Component(s):** Component(s) that assist(s) the Lead Component in developing the guidance or regulation

### **3. POLICY.**

It is FDA policy that guidance and regulation efforts led by one of the three medical product Centers or OCP (“Lead Component”) will include staff members from the other Component(s) (“Consulting Component(s)”), as appropriate, when the guidance or regulation pertains to combination products.<sup>3</sup> The engagement of any such Consulting Component(s) should be timely and the level of participation should be appropriate to ensure identification of concerns. The Federal Register notices announcing regulations and guidance and the guidances themselves should clearly indicate the Components involved in the development of the policy.

### **4. BACKGROUND.**

Policy pertaining to combination products is a growing area that requires guidance and regulation development for FDA. Combination product guidance and/or regulation often require expertise from different medical product Centers and OCP to ensure that cross-cutting regulatory matters are addressed in a comprehensive and consistent manner and that cross-cutting processes and practices are considered. Recent legislative efforts, including passage of the 21st Century Cures Act and user fee authorizations, reinforce the need for collaboration among FDA Components on policy pertaining to combination products. Although OCP is responsible for ensuring the timely, effective and aligned premarket review of combination products and their consistent and appropriate postmarket regulation, either OCP or an individual Center may initiate the development of a guidance or regulation pertaining to combination products.

### **5. RESPONSIBILITIES.**

#### Lead Component:

1. Notifies potential Consulting Component(s) of a proposal to revise an existing guidance or regulation or to develop a new guidance or regulation pertaining to combination products.
2. Engages with the Consulting Component(s) in a manner consistent with the level of participation agreed upon with the Consulting Component. As needed:

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<sup>3</sup> This procedure is aligned with, but does not replace, FDA-wide and Center procedures such as the Quality System for Regulations (see [SMG 1118.6](#)) or other Agency guidance templates.

- a. Provides timely access to documents and materials for review by Consulting Component(s).
- b. Establishes timelines for completion of deliverables related to the regulation or guidance. Timelines should take into account, whenever possible, the resource availability/capacity of the Consulting Component(s).

Consulting Component(s):

1. Reviews the consulting request from the Lead Component and determines whether the Consulting Component(s) need to participate in this activity.
2. Identifies and approves the staff members, if any, to support the regulation or guidance effort of the Lead Component.
3. Participates actively in Lead Component regulation or guidance workgroups, when such level of participation has been agreed upon between Components.
4. Provides timely review of documents as requested by the Lead Component and consistent with the level of participation agreed upon with the Lead Component.

**6. PROCEDURES.**

**A. When should the Lead Component contact another Component to determine whether there is a need to engage that Component in a regulation or guidance development effort?**

1. The need for engagement and the level of participation with other Components should be considered at the initiation phase for a regulation or guidance that pertains to a combination product. The Lead Component should contact all Components that will be or may be impacted by the regulation or guidance effort. See Section C below for additional discussion of “level of participation.”

**B. What is the process for contacting and coordinating with potential Consulting Components?**

1. The Lead Component should notify each potential Consulting Component of the need to engage in a regulation or guidance effort pertaining to a combination product. The contact list below should be

used for the initial communication, which should include the desired level of participation, expertise needed, and anticipated timeframe.

Contact List:

CBER: [CBERDocDist@fda.hhs.gov](mailto:CBERDocDist@fda.hhs.gov)

CDER: [CDER-ORPRequests@fda.hhs.gov](mailto:CDER-ORPRequests@fda.hhs.gov) with cc to [CDERProductJurisdiction@fda.hhs.gov](mailto:CDERProductJurisdiction@fda.hhs.gov)

CDRH: [CDRHOCDClearanceTracker@fda.hhs.gov](mailto:CDRHOCDClearanceTracker@fda.hhs.gov) with cc to [CDRHProductJurisdiction@fda.hhs.gov](mailto:CDRHProductJurisdiction@fda.hhs.gov)

OCP: [combination@fda.gov](mailto:combination@fda.gov)

2. The Lead Component and potential Consulting Component(s) should agree on what, if any, expertise is needed from the Consulting Component.
3. The deadline for completing the regulation or guidance effort should be set by the Lead Component. Where possible, the Consulting Component(s) should be given a minimum of 30 days to review unless a shorter timeframe is justified. If the Lead Component deadline does not provide sufficient time to complete the review, the Consulting Component and Lead Component should agree on an alternative timeframe. (see below).
4. The Lead Component should discuss the timeframes with the Consulting Component and take into account the Consulting Component's resource availability/capacity of the Consulting Component(s) when establishing timeframes for the guidance or regulation effort, to the extent this is feasible in light of the circumstances (e.g., whether the action is needed to address a public health emergency or other priorities beyond the control of the Lead Component, such as compliance with statutorily imposed deadlines).

**C. What participation by Consulting Components and public documentation of their participation are appropriate?**

1. The Lead Component and Consulting Component(s) should determine early in the development process the level of participation appropriate to enable Consulting Component(s) to provide timely, informed input on issues related to their expertise and responsibilities.

Examples of a Consulting Component's engagement include:

- Determining that participation in the effort is not necessary
- Participating regularly in a workgroup
- Drafting specific content for the guidance or regulation
- Consulting on and/or reviewing guidance or regulation content generated by the Lead Component
- Clearing the regulation or guidance

With the agreement of the Lead Component and Consulting Component(s), a Consulting Component can be included in the clearance process without having to participate otherwise in development of the regulation or guidance, if such limited engagement will enable the Consulting Component to engage effectively and in a timely manner.

2. The staff participating for a Consulting Component should be approved at the level of an Office director or higher, or designee(s). The staff participating from a Consulting Component are the Consulting Component's representatives and, as such: (i) are expected to present the views of the Component on policy matters relevant to that Consulting Component, and (ii) are responsible for obtaining timely input from appropriate policy leads in their Component while participating in development of the guidance or regulation.
3. Depending on the level of participation by the Consulting Component(s), extent of reliance on that Component's expertise, and/or the significance of the impact the regulation or guidance has on the Consulting Component(s), the name of the Consulting Component(s) should be:
  - Listed on the cover page for a guidance, and/or
  - Listed in the body of the Federal Register notice for a guidance or regulation, and/or
  - Identified in a footnote in the guidance or regulation (stating, for example, "This [guidance][regulation] has been prepared by the [Lead Component] in consultation with [name of the Consulting Component(s)].")

4. Unless the Lead and Consulting Component(s) have agreed that no participation is needed,<sup>4</sup> the Lead Component will obtain formal clearance from the Consulting Component(s) in the Federal Register Document Tracking System (FRDTS), or its successor system.

**7. EFFECTIVE DATE.**

The effective date of this guide is March 27, 2018.

**8. Document History - SMG 4103, Expectations and Procedures for Engagement Among Medical Product Centers and Office of Combination Products on Regulations and Guidance Pertaining to Combination Products**

<b>STATUS (I, R, C)</b>	<b>DATE APPROVED</b>	<b>LOCATION OF CHANGE HISTORY</b>	<b>CONTACT</b>	<b>APPROVING OFFICIALS</b>
Initial	03/26/2018	N/a	Office of Combination Products (OCP)	Rachel Sherman, FDA Principal Deputy Commissioner

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<sup>4</sup> Such agreement may be case-by-case or categorical, approved at the Office director or equivalent level.