Combination Product Process Developments

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Topics

- Combination products developments in brief
- Combination Products Council
- Section 3038 of 21st Century Cures

Developments in brief

- Final rule on postmarketing safety reporting
  - Application-related PMSR plus called out requirements
  - Compliance date for call-outs, July 2018
- Final guidance on CGMPs
  - Addressing stakeholder questions
  - Availability of different approaches to compliance
- Draft guidance on human factors
  - Efforts to ensure consistency and coordination
  - Relationship to other user interface-related policy activities

Devt's cont'd

- Intercenter consult process pilot
  - Updating processes and training
  - Pilot status

- Pre-RFD draft guidance
  - Non-binding feedback on classification/assignment issues
  - Interactive alternative/preliminary to RFD

Cures Section 3038

- Product classification and assignment
- Premarket Review
- Postmarket Regulation
- Other

Cures—Classification & Assignment

- Primary mode of action standard and assignment
- Designation justification
- Development and consideration of new data

Cures—Premarket

- Combination products agreement meetings (CPAMs) and guidance on CPAMs and pre-submission interaction
- Risk-based approach
- Leveraging, reliance and application of patent and data/marketing exclusivities
- Intercenter coordination, alignment and point of contact
- One vs. two applications

Cures—Postmarket/Other

- Postmarket regulation:
  - CPAM process
  - CGMP flexibilities listing
- Other
  - Identification of product as combination product in sponsor submissions
  - Additional Congressional report data elements

Combination Products Council

- Senior-level forum to address combination product policy
- Chaired by the Deputy Commissioner for Medical Products and Tobacco or his/her designee, and includes the Center Directors for CBER, CDER, and CDRH and the Office Director for OCP, or their designees
- Charter available at: Combination Products Council charter: https://www.fda.gov/downloads/AboutFDA/ReportsManualsForms/StaffManualGuides/UCM528113.pdf

CPC cont'd

- The Council members identify regulatory and scientific policy issues to address
- In addition to combination products, the Council can address other products intended for combined use with one another and classification of medical products
- The Council can help resolve disagreements among Centers, the Office of Combination Products (OCP), and/or sponsors (the Council does not meet directly with sponsors)

CPC Cont'd

Docket on topics for Council consideration

- Issues not appropriate for other channels
- Comment period closed April 13
- 5 sets of comments received
- OCP mailbox
- https://www.federalregister.gov/documents/2017/01/13/2017-00646/suggestions-recommendations-and-comments-for-topics-that-may-be-considered-by-the-food-and-drug

General observations/take-aways

- Focus on efficiency, consistency and coordination
- Commitment to a risk-based approach
- Commitment to speaking with one voice
- Desire to hear from you and work together
- Looking to OCP as a resource

Contacting OCP

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Combination Products: Process and Opportunities

James Boiani, MS, JD
Epstein Becker & Green, P.C.
May 5, 2017

Keep in Mind

The opinions expressed herein are my own.

21st Century Cures

Changes to the RFD Standards – Response to *Prevor*

- FDCA 503(g)(1)(E): "In determining the primary mode of action of a combination product, the Secretary shall not determine that the primary mode of action is that of a drug or biological product *solely* because the combination product has any chemical action within or on the human body."
- Establishes a new process for dispute resolution to complement 21 C.F.R. 10.75.
  - Allows for sponsors to "propose one or more studies (which may be nonclinical, clinical, or both) to establish the relevance, if any, of the chemical action in achieving the primary mode of action of such product."
  - Directs FDA and sponsor to work toward agreement on such studies.
  - *This is an important area for guidance development*

21st Century Cures

Least Burdensome Standards Officially Come to Combo Products

- FDCA 503(g)(3): "For purposes of conducting the premarket review of a combination product that contains an approved constituent part . . . the Secretary may require that the sponsor of such combination product submit to the Secretary only data or information that the Secretary determines is necessary to meet the standard for clearance or approval, as applicable, under this Act or the Public Health Service Act, including any incremental risks and benefits posed by such combination product, using a risk-based approach and taking into account any prior finding of safety and effectiveness or substantial equivalence for the approved constituent part relied upon by the applicant . . .
- *This is another key area for guidance development – reliance/bridging in the context of combo products is often an areas of concern for developers due in part to differences of Center philosophies*

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OCP's Formalized Role in the Review of Combo Products

- FDA 503(g)(8)(A)(i) – OCP "shall help to ensure timely and effective premarket review that involves more than one agency center by coordinating such reviews, overseeing the timeliness of such reviews, and overseeing the alignment of feedback regarding such reviews."
  - Formalizes a role OCP has played informally in the past
  - Gives in more directed tasks to manage in terms of coordinating reviews and assuring consistency across Centers

Beyond the 21st – Appeals

Appeals above OCP regarding RFD decisions

- Currently no timeline for reaching decisions (unlike almost all other decisions)
- At least one appeal has been pending for two years
- March 2017 Citizen Petition calls on FDA to adopt reasonable timelines to hear appeals
  - *Even with the new dispute resolution processes, 21 CFR 10.75 appeals are still the route to review of decisions above OCP*
  - *A **great** petition to write a letter of support for… Docket No. FDA-2017-P-1391.*

Beyond the 21st – Human Factors

Draft Human Factors Guidance for Combination Products

- A **tremendously** important issue for drug/biologic + device combination products
- Traditionally there have been two very different philosophies regarding assessments
  - Understanding usability through human factors engineering validation (see CDRH Guidance)
  - Understanding usability through actual use/clinical trial testing
- *If you have not submitted comments on the draft yet, you should still consider doing so because the guidance could have a major effect on product development*

Beyond 21st Century Cures

Wound Care Products

- Meeting in September 2016 to discuss classification of various wound coverings that contain silver or other substances
- FDA is looking at potential reclassification of products
  - May be driven in part by CDER actions regarding antimicrobial soaps and aligning evidentiary standards across Centers
- From a public health and policy perspective, the issues that FDA is thinking about in wound care have broad applicability to combo products and is something you should watch closely and engage in if you have interest in *any* combo products

Opportunities in Combination Products

Lifecycle management

Are we moving away from "drug product" approvals to "treatment system" approvals?

- Example: Drug delivery systems
  - Novel drug delivery systems are being developed to add assurance of safe and effective use
  - The standards being applied to assessment of these systems are increasing
    - What was previously more of an engineering / human factors evaluation exercise is now transforming into actual use studies with products
- Example: Mobile devices
  - Interest in new technologies to monitor patients, assure compliance, adjust dose
  - If embedded in pivotal trials, they may be part of the conditions for approval

Could patents on these ancillary products provide additional, indirect, avenues of protection for drug products?

Thanks for listening!

- *If you have any questions or complaints, give me a shout*
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