NCI Optical Imaging Workshop

Regulatory Pathway Considerations for Optical Imaging Drugs and Devices Used Together

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Discussion Topics

• Pathway to market: blending the drug and device development

• Are optical imaging drug and devices combination products or not?

• What are the developmental implications?

• What practical considerations?
Imaging Drugs in General

• Most general imaging drugs are not combination products

  • But there are some exceptions
Optical Imaging Pathway to market

- Device alone?
- Drug alone?
- Device or Drug with limited reference labeling?
- Device - Drug with full reference to each other?
Separately Provided Products: Labeling Jargon

• General labeling: Broad use; does not restrict to a particular drug or device

• One-way labeling:
  • Brand Drug A for use with Brand Device A
  • Brand Device A for use with drugs with certain characteristics

• Two-way labeling (cross-labeling; combination Product)
  • Brand Drug A for use with Brand Device A
  • Brand Device A for use with Brand Drug A
Consistency Consideration for Safety & Effectiveness Labeling

- Indication for Use: differs from approved / cleared labeling
- Drug changes:
  - Dose, rate, route or method of administration; dosing regimen or frequency
  - Imaging method differences
- Device changes:
  - Modality or exposure differences,
  - Cleared for use with different drug
- Safety or other labeling revisions for new use
What is a combination product?

• Combination product comprises 2 or more differently classified products*
  
  • Drug + Device
  • Device + Biologic
  • Drug + Biologic
  • Drug + Device + Biologic

*21 CFR Part 3
Combination Product: Definition

• **21 CFR Part 3**
  
  • Physically or chemically into a single entity; §3.2(e)(1)
  
  • Co-packaged (Kit); §3.2(e)(2)
  
  • Sold separately and **labeled for use together**; §3.2(e)(3) or (e)(4)
• (e)(3) A drug, device, or biological product packaged separately that according to its investigational plan or proposed labeling is intended for use only with an approved individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect and where upon approval of the proposed product the labeling of the approved product would need to be changed, e.g., to reflect a change in intended use, dosage form, strength, route of administration, or significant change in dose; or

• (e)(4) Any investigational drug, device, or biological product packaged separately that according to its proposed labeling is for use only with another individually specified investigational drug, device, or biological product where both are required to achieve the intended use, indication, or effect
Assignment / Jurisdiction of CP

- Combination Product (CP)
  - CDER, CBER, or CDRH
  - Assigned based on the primary mode of action (PMOA)* or algorithm**

*FD&C Act, Section 503(g);
**21 CFR 3.2(m)
Assignment / Jurisdiction of CP, Cont’d

• Mode of Action (MOA) – “the means by which a product achieves its intended therapeutic effect or action, …” § 3.2(k)
  • Action is based on the drug, device, biologic definitions

• PMOA – “the single mode of action of a combination product that provides the most important therapeutic action …
  • Most important therapeutic action is the mode of action expected to make the greatest contribution to the overall intended therapeutic effects…” § 3.2(m)
Useful Assignment Information

• Guidance documents and regulation*
  • PMOA Rule, 21 CFR Part 3 revision – 2005
  • Chemical Action (draft) – 2011
  • Classification (draft) – 2011
  • How to Write an RFD - update 2011

* http://www.fda.gov/CombinationProducts/default.htm
What does it mean when CP is assigned?

- Lead center for industry contact
- Collaborative review with other center experts
- Product is still a combo once assigned, does not change classification to that of the type of products customarily in that center.
- Must comply with applicable regulations / requirements of both constituent parts without being contrary or confounding.
Combination Product: General Regulatory Approach

• Premarket
  • Apply consistent standards to assess safety and effectiveness regardless of Center assignment
  • Use consistent and appropriate regulatory pathways
  • One investigational application (i.e., the one used by the lead center)
  • One marketing application for most combination products but might vary based on the marketing configuration

• Postmarket
  • Compliance with regulatory requirements for each constituent part while avoiding redundancy
  • Ensure consistent compliance and inspectional standards
  • Ensure consistent standards and pathways for postmarket changes
What is similar regardless of combination or non-combination status?

- Centers continue to work together to
  - Determine if the product is appropriately classified and in the appropriate center
  - Identify and assess the scientific and technical data
  - Consider the labeling that is appropriate to ensure safe and effective use of the product(s) for the proposed indication
  - Achieve consistency and transparency
Contact Us –
We’re Here to Help!

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