510(k), De Novo, or PMA Combination Product with a Drug/Biologic Constituent Part

Moderator: Quynh Hoang, Senior Regulatory Consultant, King & Spalding LLP

FDAnews Combination Products Conference, June 8, 2017
Outline

1. Introduction
2. “Any chemical action” and PMOA
3. Thought Exercises
4. Section 505(b)(2) Requirements
Introduction

➤ Sugato De
   Principal Consultant, Parexel International

➤ Janine Morris
   Vice President, Global Regulatory Affairs | Devices
   Eli Lilly and Company

➤ Elaine Tseng
   Partner, King & Spalding LLP
“ANY CHEMICAL ACTION” AND PMOA
“Any chemical action” and PMOA

Drug Definition

A. Articles recognized in the official United States Pharmacopoeia, Homeopathic Pharmacopoeia of the United States, or official National Formulary, or any supplement to any of them;

B. Articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animal; and

C. Articles (other than food) intended to affect the structure or any function of the body of man or other animals.

FDCA 201(g)
“Any chemical action” and PMOA

Device Definition

An instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is –

1) recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
2) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or
3) intended to affect the structure or any function of the body of man or other animals,

And which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes.

FDCA 201(h)
“Any chemical action” and PMOA

Biologic Definition

- Virus
- Therapeutic Serum
- Toxin or Antitoxin
- Vaccine
- Blood, Blood Component or Derivative
- Allergenic Product
- Protein (except any chemically synthesized polypeptide)
- Analogous product (e.g., cell and gene therapies, probiotics)
- Arsphenamine or its derivatives (or any other trivalent organic arsenic compound),

applicable to the prevention, treatment, or cure of a disease or condition of human beings.

PHSA 351(i)
“Any chemical action” and PMOA

Combination Product Definition

– Combination of
  ▪ Device & Biologic
  ▪ Device & Drug
  ▪ Drug & Biologic
  ▪ Biologic & Device & Drug

– Combination meaning
  ▪ Physically or chemically combined (single-entity)
  ▪ Co-packaged in a kit
  ▪ Physically separate, but cross-labeled

21 CFR 3.2(e)
“Any chemical action” and PMOA

Primary Mode of Action (PMOA) Definition

The single mode of action of a combination product expected to make the **greatest contribution** to the overall intended therapeutic effects of the combination product.

FDCA 503(g)(1)(C), 21 CFR 3.2(m)
“Any chemical action” and PMOA

Algorithm for assigning lead Center for a Combination Product

A. PMOA

B. If unable to determine PMOA,
   1. Consistency
   2. Expertise

21 CFR 3.4
“Any chemical action” and PMOA

Example:

Information Brochure from [http://www.medicalcare.se](http://www.medicalcare.se), retrieved on June 5, 2017
“Any chemical action” and PMOA

• New statutory provision:

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.

21st Century Cures Act, sec. 3038(a)(4) (FDCA 353(g)(1)(E))
“Any chemical action” and PMOA

Example: Catheter with drug/biologic coating

“Any chemical action” and PMOA

Example: Material with drug/biologic

https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-afda-adcom/documents/document/ucm518494.pdf,
Retrieved on May 29, 2017
THOUGHT EXERCISES
Thought Exercise #1

The product is a surgical hemostat patch intended to control bleeding and serve as barrier for infection.

- Supportive Layer: Non-woven synthetic polymer with thrombin powder
- Adhesive Layer: Fibrinogen powder with quick-dissolving polymer additive
Thought Exercise #1 (Cont.)

1. What Center would likely regulate this product?
2. What Center would likely regulate the product if there was only the supportive layer?
3. How would categorization in CBER vs. CDRH affect differences in regulatory requirements?
4. What types of combination products that involve drug/biologic constituents may be approved in CDRH?
Thought Exercise #2

The antimicrobial constituent is identified in the 510(k) submission along with clear statements that it is intended to reduce colonization on the device constituent and has not been confirmed to prevent/treat infection in patients. Bench tests demonstrate reduction in colonization and equivalent performance to the predicate device (not a combination product).

Will FDA likely request clinical data, if
1. the antimicrobial is in the coating of the device?
2. the antimicrobial is in the materials that form the device?
Thought Exercise #3

The combination product was cleared with a single drug constituent in its coating. Due to supplier change, need to switch to a coating that has two drugs.

Can the change be implemented with a letter-to-file, if the same bench/animal studies that were used to support the cleared 510(k) also demonstrate that the new coating is well within the specifications of the old coating?
SECTION 505(B)(2) REQUIREMENTS
Section 505(b)(2) Requirements

Approved Drug Constituent in a 510(k), De Novo or PMA Submission

➢ Patent certification(s),
➢ Notice of Paragraph IV patent certification, and
➢ Timing of 510(k) clearance, De Novo classification or PMA submission/approval
Thanks!
TIME PERMITTING, ADDITIONAL THOUGHT EXERCISES
Thought Exercise #4

For a device constituent that was approved as a part of an NDA/BLA,

1. Are there benefits to separating out the device constituent and submit a device-only submission to CDRH?
2. What type of submission -- 510(k), De Novo or PMA?
3. What questions to expect from CDRH?
Thought Exercise #5

The drug constituent is intended to be a preservative to allow for multi-uses of the combination product. The intended use statements, indications and the rest of the labeling for the combination product do not make any claim associated with drug constituent.

1. Should the sponsor have a pre-submission meeting with FDA?
2. What questions to ask FDA?