



# CDRH/ODE Perspectives on Adding Anti-biofilm Technologies/Agents to Devices

Biofilms, Medical Devices and Anti-Biofilm Technology  
– Challenges and Opportunities Workshop

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# Overview

1. Current landscape
2. Regulatory challenges
3. Combination product regulation

# Carrying out CDRH's Mission

- Protect and Promote Public Health by:
  - Expediting approval/clearance of safe and effective medical devices to patients
  - Utilizing evidence-based decision making
  - Determining appropriate benefit/risk profile

# Biofilms: CDRH perspective

- Indications/claims vary in regulatory submissions
- Defined by:
  - Confirmed presence?
  - Explicit intended use to reduce, treat, prevent?
  - Implied claims?
- Lack of precise terminology
  - Colonization → biofilms → infection

## Indications/Claims in Regulatory Submissions

- “controlling biofilm and microbial counts”
- “penetrate and remove biofilm”
- “help prevent biofilm formation”
- “biofilm removal and degradation”
- “reduction of biofilm”
- “inhibit bacterial colonization”
- “affects the growth of biofilm formation”

How does this translate to  
clinical outcomes?

What does this mean for the  
patient?

# Biofilms: CDRH Perspective

- Lack of standardized testing
  - No recognized assay to evaluate amount of biofilm or what constitutes a clinically meaningful reduction in biofilm
  - No corollary to USP Preservative Assay used to evaluate antimicrobial-preservative effectiveness
- No CDRH standards or guidances
- Types of anti-biofilm technologies reviewed by CDRH has been limited

# Examples of Device Types with Antimicrobials

- Wound dressings
- Wound irrigation solutions
- Catheters (e.g., urinary, hemodialysis)
- Surgical mesh
- Bone cement
- Endotracheal tubes



# Examples of Drugs/Antimicrobials

- Silver
- Silver sulfadiazine
- Zinc oxide
- Chlorhexidine
- PHMB
- Gentamicin
- Tobramycin
- Plant extracts

# Current Practices

- Indications for use should include indications for antimicrobial agent
- Rationale for adding the antimicrobial agent
- Characterization of the antimicrobial agent
- Performance testing of medical device + antimicrobial agent

# Regulatory Challenges

- What is the optimal benefit/risk profile?
  - Potential clinical benefit of the use of an antimicrobial agent on a medical device should outweigh the associated risk
  - How do we assess clinical benefit?
  - How do we assess potential antimicrobial exposure of all patients (100%) for an infection that may only occur in 1.0% of patients
  - Do we factor in public health concerns related to antimicrobial resistance?

# Regulatory Challenges

- Demonstrating clinical benefit may be impractical
  - Medical device + antimicrobial vs. device alone
  - Extremely large clinical studies may be needed to demonstrate indications/claims such as prevention or reduction of biofilm/colonization/infection

# Regulatory Challenges

- How do we create consistency to ensure that meaningful and accurate information is communicated in labeling?
  - Definitions, terminology
  - Data necessary to support indications/claims

# Regulatory Challenges

- Jurisdiction
- Disparity in statutory and regulatory requirements between CDRH & CDER/CBER
- Off label use of drugs/biologics
- Learning curves – FDA and industry
- Appropriate leveraging of available information

# Jurisdiction: Devices vs. Drugs

## Gauze Wound Dressing with Silver Coating



# Combination Products

- Most medical devices + antimicrobials are combination products
  - Definitions – devices, drugs, combination products
  - What am I? Where do I go?
  - PMOA and the RFD process
  - Office of Combination Products



# What is a Combination Product?

- **Drug + Device**
- Device + Biologic
- Drug + Biologic
- Drug + Device + Biologic
- $\neq$  Drug + Drug; Device + Device; Biologic + Biologic
- They can be:
  - **Physically or chemically combined**
  - Co-packaged in a kit
  - Separate, cross-labeled products

# Definition of a Drug

- The term "drug" means:
  - (A) articles recognized in the US Pharmacopoeia, Homeopathic Pharmacopoeia, or National Formulary;
  - (B) articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease in man or other animals;
  - (C) articles (other than food) intended to affect the structure or any function of the body of man or other animals.

# Definition of a Device

- Instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is -
  - recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them
  - 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
  - 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.

# To Summarize:

- The drug definition is the broadest
- The drug and device definitions address:
  - What a product is intended to do
  - How a product works (device cannot achieve its primary intended purposes through chemical action or by being metabolized)



# If I am a combination product...



# Primary Mode of Action (PMOA)

- The Office of Combination Products (OCP) determines which FDA Center will have primary jurisdiction based on PMOA
- Primary mode of action is the **single mode of action** of a combination product that provides the most important therapeutic action of the combination product. The most important therapeutic action is the mode of action expected to make the **greatest contribution to the overall intended therapeutic effects** of the combination product.

# PMOA Algorithm

If PMOA cannot be determined with reasonable certainty, consider:

1. **Consistency:** is there an agency component that regulates other combination products presenting similar questions of S&E with regard to combination product as a whole?
2. **Safety and Effectiveness:** which agency component has the most expertise related to most significant S&E questions presented by combination product?

# PMOA: CDER or CDRH?

## Gauze Wound Dressing with Silver Coating

- Indication: wound covering and prevention of bacterial colonization within the wound dressing
- Primary action – dressing provides a barrier, absorbs exudate, maintains moisture
- Secondary action – silver prevents biofilm formation in the dressing so that dressing does not become a nidus for infection

Regulated in CDRH

- Indication: treatment of infected wounds
- Primary action – silver acts in the wound to treat active infection
- Secondary action – dressing provides local delivery of silver to wound

Regulated in CDER



# Pathways to Market

CDRH	CDER
<b>Approval to begin Clinical Evaluation</b>	
<b>IDE</b> <b>Investigational Device Exemption</b>	<b>IND</b> <b>Investigational New Drug</b>
<b>Permission to begin Marketing</b>	
<b>PMA</b> <b>(Class III Devices)</b>	<b>NDA</b> <b>New Drug Application</b>
<b>510(k)</b> <b>Premarket Clearance</b>	<b>ANDA</b> <b>Abbreviated NDA</b> <b>Generic Drug Application</b>

# Request for Designation (RFD)

- Voluntary Formal Process (21 CFR Part 3)
- Binding determination:
  - Classification (what am I?)
  - Assignment (where do I go?)
  - Clarification of Regulatory Pathway (what do I do when I get there?)
- An RFD should be filed when the classification or assignment of a product is unclear or in dispute

# Why Does Jurisdiction Matter?

- FDA wants to provide the best possible regulatory and scientific advice to sponsors as early as possible in the product development process
  - Get the right staff involved early
  - Gain understanding of regulatory landscape
  - Work through complex scientific and regulatory issues with FDA

# Office of Combination Products

- OCP has broad combination product responsibilities, including classification and jurisdiction
- Contact Information:

Office of Combination Products

Phone: 301-796-8930

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

Online: <http://www.fda.gov/CombinationProducts/default.htm>

# Final Thoughts

- There are many regulatory and scientific challenges FDA faces in the regulation of medical devices with antimicrobial drugs.
- Scientific discourse and research can inform regulatory decision making.



# CDRH is Here to Help

- Division of Small Manufacturers, International and Consumer Assistance (DSMICA)
  - Email: [dsmica@fda.hhs.gov](mailto:dsmica@fda.hhs.gov)
  - Phone: 1-800-638-2041
- Work with FDA review staff through the Pre-submission process
  - Pre-Sub and Meetings Guidance:  
<http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf>

# Thank You!



Questions? Comments?

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