

# CDER Product Jurisdiction Team

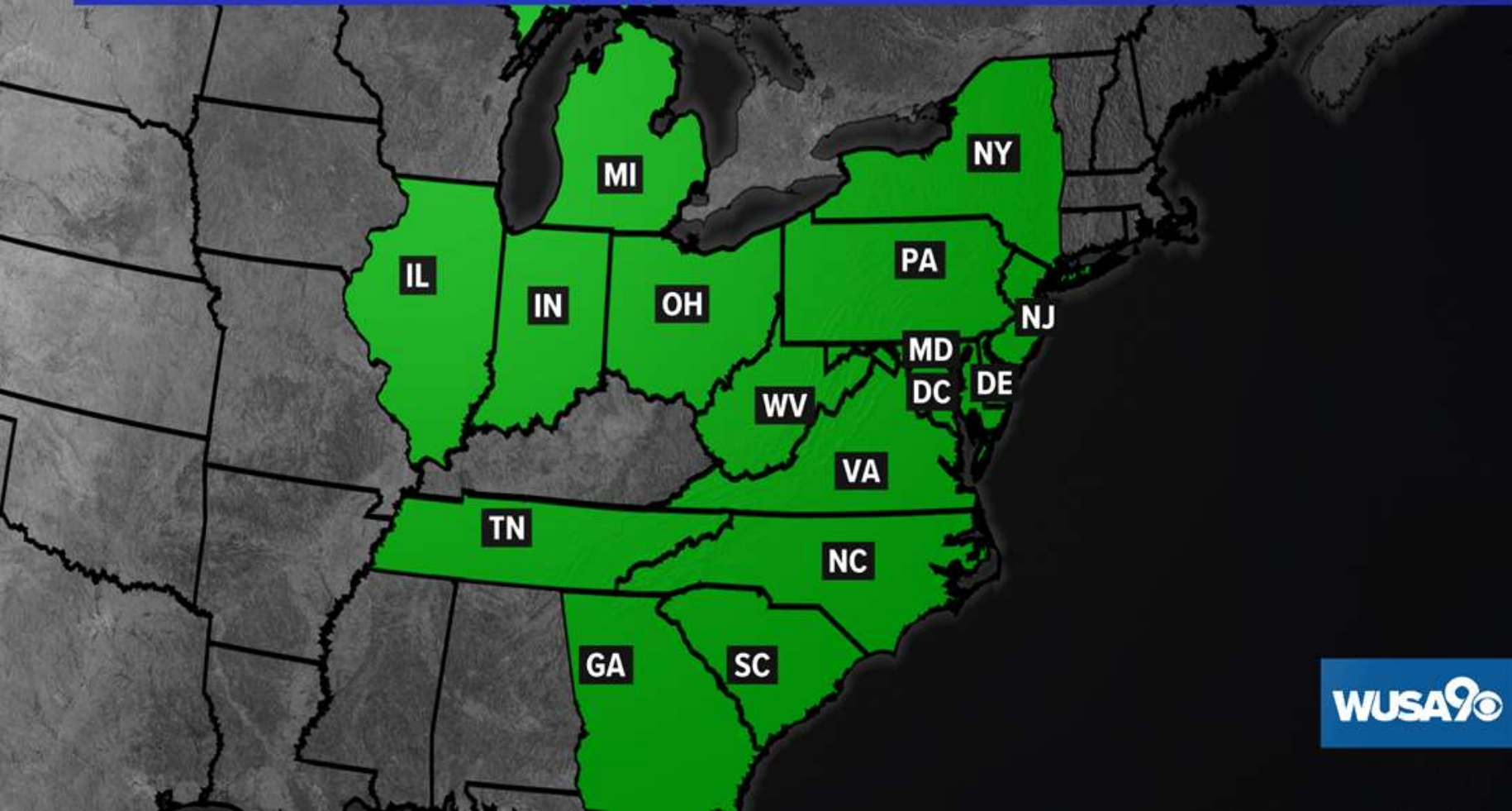
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Combination Product Policy Advisor

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CDER | US FDA

## CICADAS 2021 MAY TO JUNE



# Learning Objectives



- Learn about the cicada lifecycle
- Tell bad cicada jokes
- .....



# Learning Objectives



- Understand the role of the CDER Product Jurisdiction Officer (PJO)
- Describe the Agency's assignment of combination products
- Identify best practices for interacting with CDER on combination products



# Who are the CDER PJOs?



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# What do we do?



- CDER focal point for any classification, jurisdiction or combination product questions or issues
- CDER's liaisons to the Office of Combination Products (OCP)
- Represent CDER on combination product and jurisdiction policies and procedures



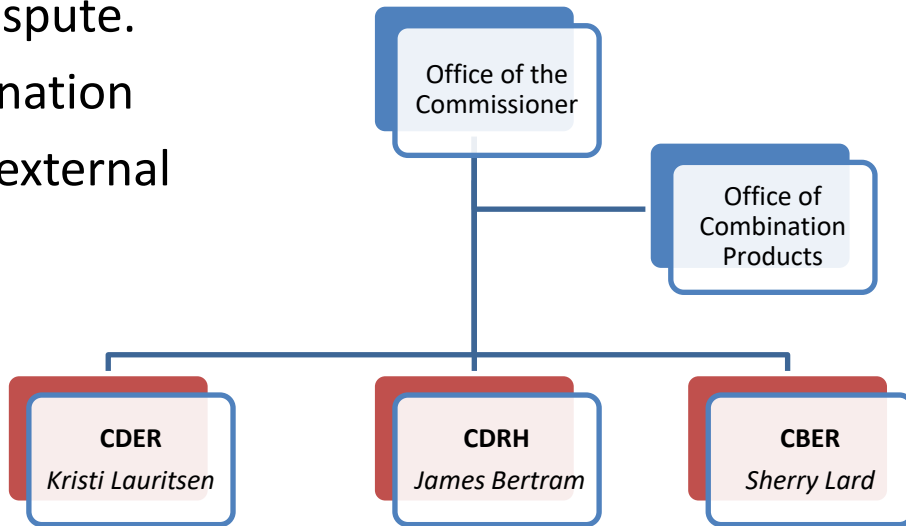
# What does that mean?

- Work with OCP to develop guidance documents and regulations
- Represent CDER-level position in inter-center working groups
- Help sponsors clarify the regulatory pathway for products assigned to CDER
- Respond to internal and external inquiries



# Office of Combination Products (OCP)

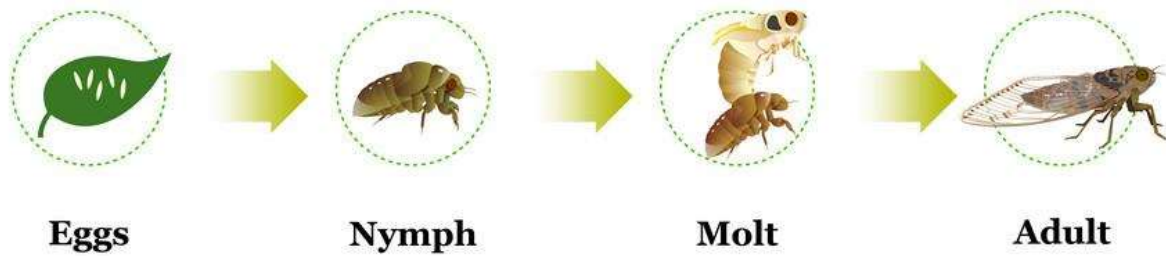
- Authority to assign an FDA center to have primary jurisdiction for review of both combination and single entity (i.e., non-combination) products where jurisdiction is unclear or in dispute.
- Agency focal point for combination product issues for internal / external stakeholders
- Broad oversight responsibilities covering the regulatory life cycle of combination products



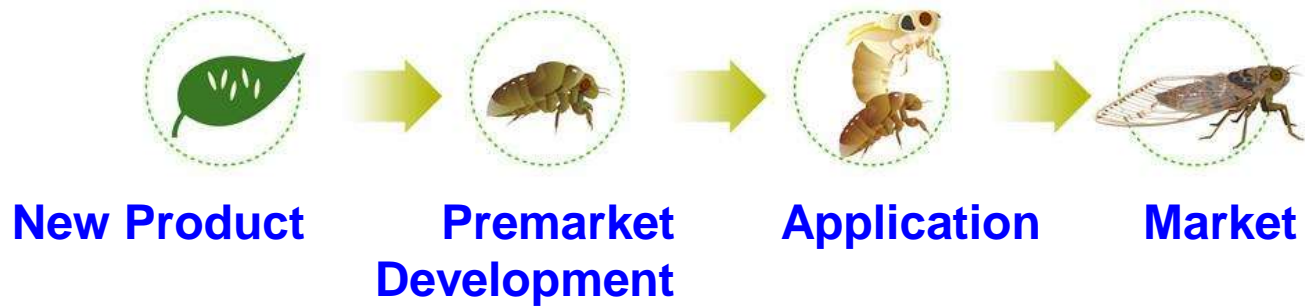
# OCP vs CDER PJO

OCP Role	CDER Role
Assign combo and non-combo products to a lead Center	Provides CDER's position on combo, non-combo, and jurisdiction
Focal point for internal/external stakeholders for CDER, CDRH and CBER	Focal point for CDER stakeholders – CDER Combo WG meets bi-weekly
Ensure consistent regulation of combination products in all Centers	Ensure consistent regulation of CDER-led combination products
Central ICCR oversight with CDRH, CBER and CDER	CDER ICCR coordinator
FDA focal point for cross-center process and policy	CDER focal point for regulatory process and policy issues

## Cicada Life Cycle



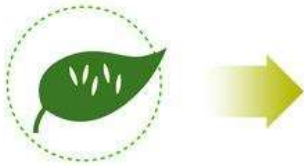
## Product Life Cycle





**New Product**

What is it  
*and*  
 Where does it go?



New Product





# What Is It?

- Drug – 201(g) FDCA<sup>1</sup>
- Device – 201(h) FDCA
- Biological Product – 351 PHSA<sup>2</sup>
- Combination Product – 503(g) FDCA, 21 CFR 3.2(e)
- Also occasionally need to consider cosmetics, foods, dietary supplements, and medical foods
- Not FDA regulated

1. Food, Drug, and Cosmetic Act

2. Public Health Service Act

# Where Does It Go?

## Non-combination Products

- Device = CDRH
- Drug = CDER
- Biological Product = CBER

## Combination Products

**\*\*Based on Primary Mode of Action\*\***

- PMOA Device = CDRH
- PMOA Drug = CDER
- PMOA Biologic = CBER or CDER

### Exceptions:

Devices that create a biologic at the point of care (devices regulated by CBER)

Therapeutic proteins, antibodies (biological products regulated by CDER)

# What if you're still not sure?

- Start with an informal email inquiry
  - OCP mailbox:
    - [combination@fda.gov](mailto:combination@fda.gov)
  - Center Jurisdiction mailbox:
    - [CDERProductJurisdiction@fda.hhs.gov](mailto:CDERProductJurisdiction@fda.hhs.gov)
    - [CDRHProductJurisdiction@fda.hhs.gov](mailto:CDRHProductJurisdiction@fda.hhs.gov)
- Submit an RFD or pre-RFD **BEFORE** any submission (i.e., presubmission / pre-IND, marketing submission)



## Why?

FDA may stay the review clock while a determination is being made (21 CFR 3.10)

# Source of Inquiries

- OCP - RFD/preRFD
- CDER reviewers (OND, OGD, OPQ, OSE)
- CDER Compliance
- CDER Division of Drug Information
- CDRH
- CBER



**New Product**



**Premarket  
Development**



# PJO Interactions During Premarket



- PJOs advise CDER staff on submission specific questions (preIND, preANDA, IND, etc.)
  - Classification – is it a combo? is the submission in the wrong Center?
  - Combination product requirements (# of submissions, GMPs, etc.)
  - Process – intercenter consults

# Intercenter Consultation



- Allow CDER to request specific input and expertise from CBER or CDRH
- CDER PJO facilitates an enhanced internal process – IT updates and resources for staff
- CDER PJO advises staff on who, when, and how to consult
- Center consultation and collaboration is ongoing throughout product life-cycle
- Lead center responsible for interactions with sponsor and consulting center



# Intercenter Consultation

**Table 18. FY 2014 to FY 2019 Inter-Center Consult Workloads.**

Submission/Request	FY 14	FY 15	FY 16	FY 17	FY 18	FY 19	FY 14 to FY 18 5-Year Average	FY 19 Compared to 5-Year Average
Total Inter-Center Consult Requests	1,013	932	1,130	1,419	1,445	1,328	1,188	+ 12%

**Table 19. Number of Premarket Review Inter-Center Consults for Combination Products by Lead and Consulted Center.**

Lead Center	Consulted Center			
	CBER	CDER	CDRH	Number of Consults
CBER	--	36	97	133
CDER	29	--	763	792
CDRH	7	396	--	403
<b>Total</b>	<b>36</b>	<b>432</b>	<b>860</b>	<b>1,328</b>



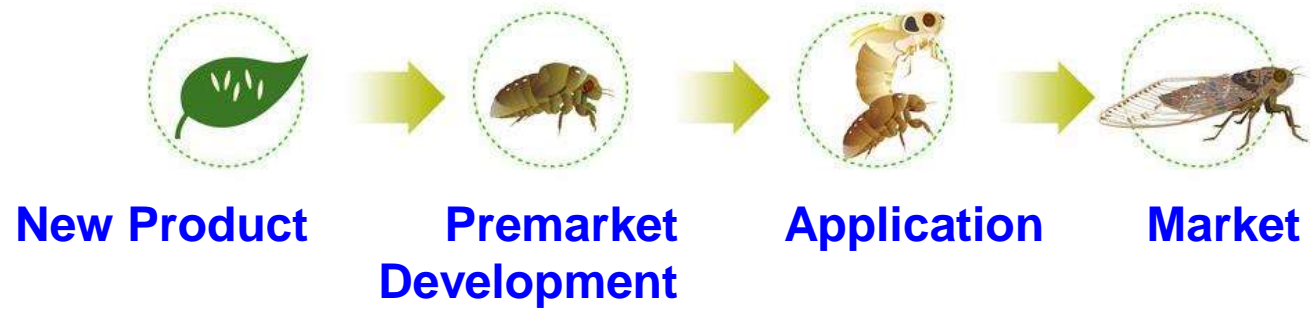
# Combination Product Premarket Submissions



- NDA - section 505 of the FDCA describes three types of new drug applications
  - 505(b)(1) – full report of safety and effectiveness
  - 505(b)(2) – full report of safety and effectiveness, *but* some data comes from studies not conducted by the applicant (e.g., published literature)
  - 505(j) - identical in active ingredient, dosage form, use, route of administration, etc., to a previously approved product (*abbreviated* NDA or ANDA) – generic drug
- BLA (original) – section 351(a) of the PHS Act
- BLA (Biosimilar) – section 351(k)

# User Fees

- No separate user fee paradigm for combination products
- Fees depend on type of application submitted (e.g., PDUFA, GDUFA, BsUFA)



# Post-Market Safety Reporting for Combos



- While PMSR regulations for drugs and devices share many similarities, each has distinct requirements. Meant to ensure consistency and completeness but avoid duplication.
- Final rule issued on 12/20/16 (81 FR 92603), and codified in 21 CFR Part 4
- Final Guidance (July 2019)

<https://www.fda.gov/combination-products/guidance-regulatory-information/postmarketing-safety-reporting-combination-products>

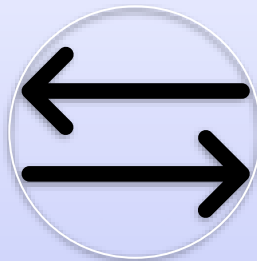




# OCP, Center, or Division?



Division



CDER PJO



OCP



# Challenge Time!



# Challenge Question 1



If a sponsor/applicant is uncertain whether their product should be regulated as a drug or a device, who should they ask?

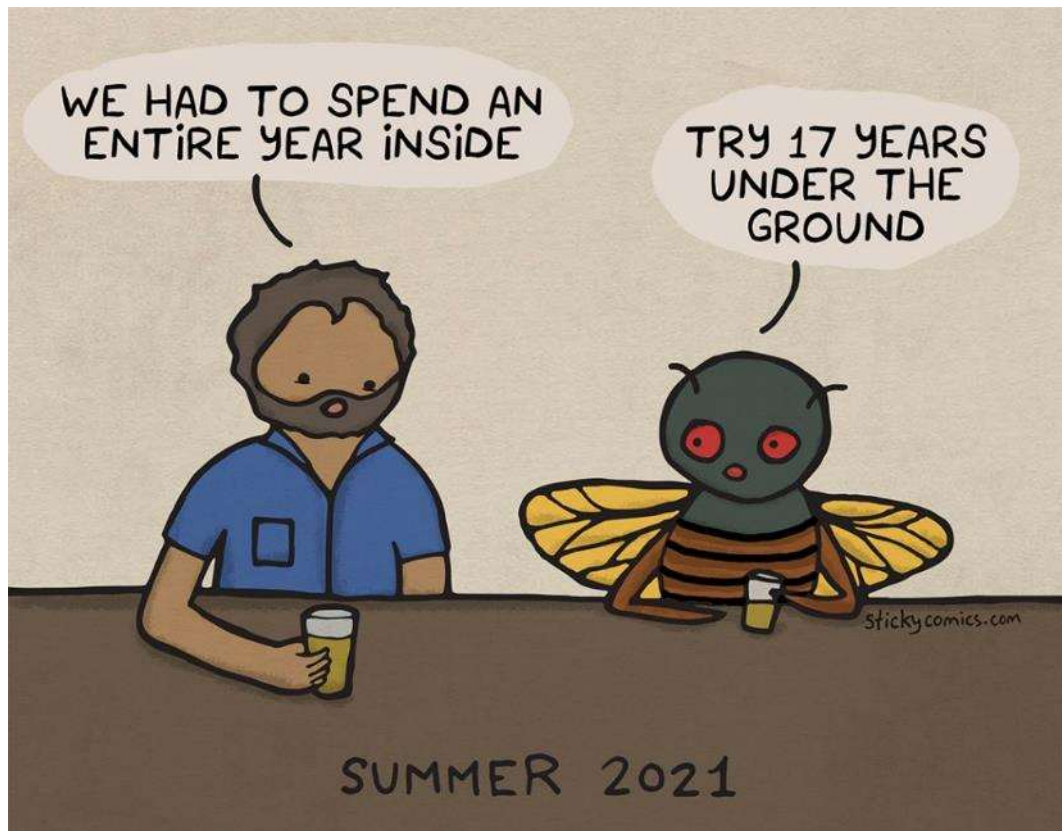
- a) CDER PJO
- b) OCP

# Challenge Question 2



If you have an approved combination product in CDER (e.g., NDA), who should you ask about the type of supplement needed for making a change to the device constituent of the combination product?

- a) OCP
- b) CDER
- c) CDRH



# Questions?

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# Industry Education Resources



## **Acts, Rules and Regulations**

<http://www.fda.gov/CombinationProducts/GuidanceRegulatoryInformation/ucm109108.htm>

## **Combination Product Guidance documents (final and draft)**

<http://www.fda.gov/RegulatoryInformation/Guidances/ucm122047.htm>

## **Office of Combination Products**

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



# Abbreviations

- AE – adverse event
- ANDA – abbreviated new drug application
- BLA – biologic license application
- CBE – changes being effected
- CBER – Center for Biologics Evaluation and Research
- CDER – Center for Drug Evaluation and Research
- CDRH – Center for Devices and Radiological Health
- CFR – Code of Federal Regulations
- cGMP – current Good Manufacturing Practices
- DES – drug eluting stent
- FDA – Food and Drug Administration
- FDCA – Food, Drug, and Cosmetic Act
- HDE – Humanitarian Device Exemption
- IDE – Investigational Device Exemption
- IND – Investigational New Drug
- IV - intravenous
- MOA – mode of action
- NME – new molecular entity
- NDA – New Drug Application
- NOAEL – no observed adverse effect level
- OCP – Office of Combination Products
- PHSA – Public Health Services Act
- PK - pharmacokinetics
- PMA – premarket approval
- PMOA – primary mode of action
- QSR – quality systems regulations
- RFD – request for designation

