# Pre-ANDA Program Overview

## Complex Generic Drug Product Development Workshop

September 12, 2018

Session 1: Overview of Pre-ANDA Program for Complex Generic Drug Products

**Lei Zhang, Ph.D.**

Deputy Director

Office of Research and Standards, Office of Generic Drugs

CDER | US FDA

# Complex Products

## A defined term in the GDUFA II Commitment Letter

- Complex active ingredients
- Complex formulations
- Complex routes of delivery
- Complex dosage forms
- Complex drug-device combinations
- Other products where complexity or uncertainty concerning the approval pathway or other alternative approach would benefit from early scientific engagement

Generic Drug User Fee Amendment (GDUFA) II Commitment Letter:
https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf

# Complex or Non-Complex Products?

## Non-complex

- Tablet, capsules, solutions and suspension for oral administration and systemic delivery
  →Solid oral modified-release (MR) dosage forms are non-complex
- Solutions for topical or parenteral administration

## Complex

- Complex active ingredients including peptides
- Complex dosage forms (e.g., long acting injectable, transdermal systems)
- All locally acting drugs
- Drug-device combinations with user interface considerations
- Abuse deterrent formulations



Generic Drug User Fee Amendment (GDUFA) II Commitment Letter:
https://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM525234.pdf

# Pre-ANDA Program for Complex Products

- Pre-ANDA Meetings
- Product Development
- Pre-Submission
- Mid-Review Cycle

# Goals of the Pre-ANDA Program Under GDUFA II

- Clarify regulatory expectations for prospective applicants early in product development
- Assist applicants to develop more complete submissions
- Promote a more efficient and effective ANDA assessment process
- Reduce the number of review cycles required to obtain ANDA approval, particularly for Complex Products

# Outline of My Presentation

## Pre-ANDA Program

1. Research
2. Guidance (Product-Specific Guidance)
3. Pre-ANDA Meeting
4. Controlled Correspondence

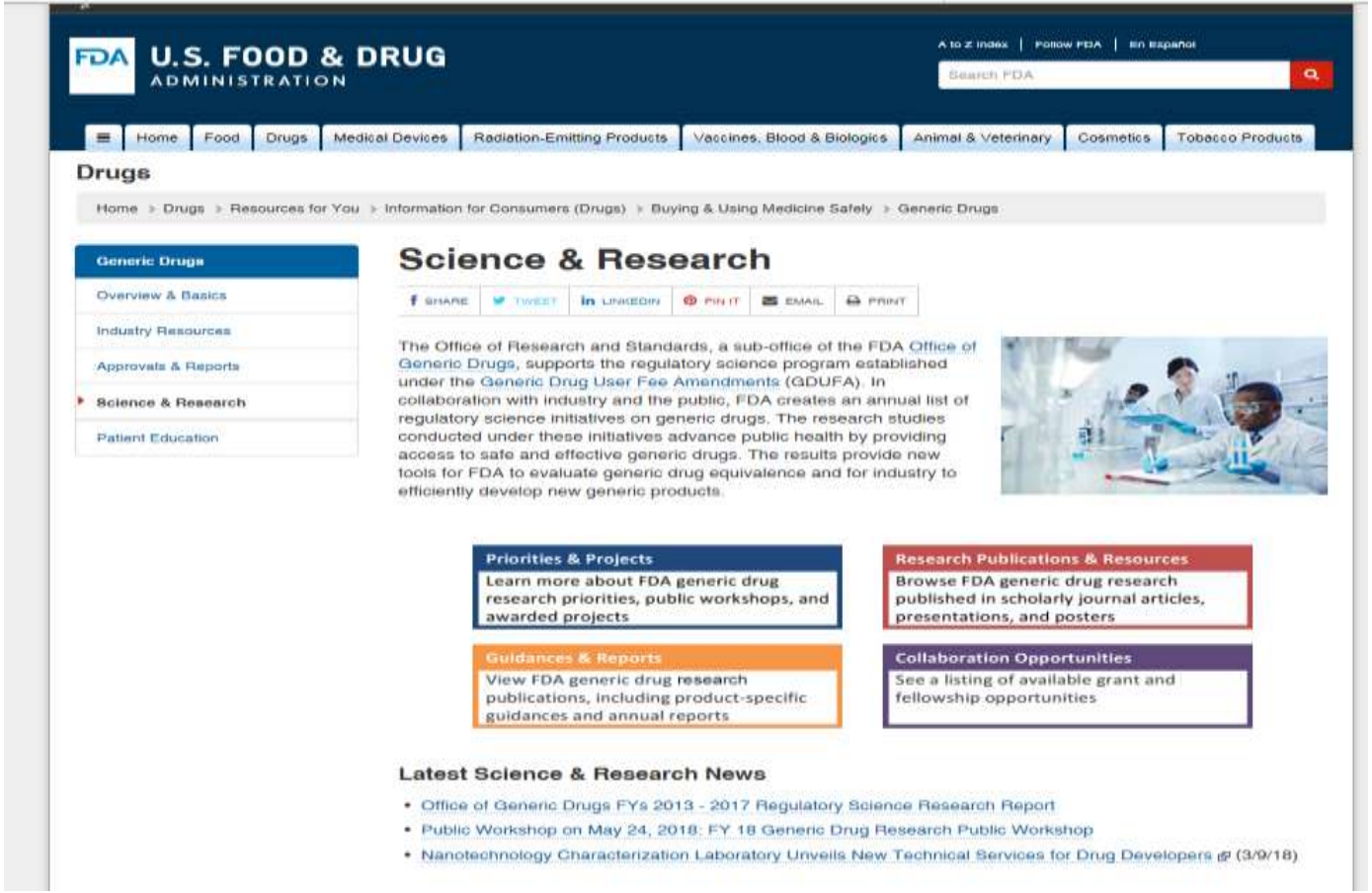
# Pre-ANDA Program for Complex Products:
# 1. Research

- Scope
  - FDA conduct internal and external research to support fulfilment of submission assessment and pre-ANDA commitments
- Public Workshops
  - Annually, FDA will conduct a public workshop to solicit input from industry and stakeholders for inclusion in an annual list of GDUFA II Regulatory Science initiatives
  - Interested parties may propose regulatory science initiatives via email to genericdrugs@fda.hhs.gov
  - After considering industry and stakeholder input, FDA will post the list on FDA's website
  - Industry GDUFA II regulatory science working group
    - Meet with FDA twice yearly on current and emerging challenges and concerns

# Pre-ANDA Program for Complex Products:
# 1. Research

- Reporting
  - Annually, FDA will report on its website the extent to which GDUFA regulatory science-funded projects
    - Support the development of generic drug products
    - Generate evidence needed to support efficient assessment and timely approval of ANDAs
    - Evaluate generic drug equivalence
- Venues for communications of results
  - Webinars and workshops ( e.g., five FDA workshops October 2017-May 2018)

# GDUFA Science and Research Website




https://www.fda.gov/drugs/resourcesforyou/consumers/buyingusingmedicinesafely/genericdrugs/ucm567695.htm

# Pre-ANDA Program for Complex Products:
## 2. Guidance

- In addition to general guidances, Product-Specific Guidances (PSGs) provide clear and direct advice to ANDA applicants

- Product-specific guidances identify the methodology for developing drugs and generating evidence needed to support generic drug approval
  - ~1,600 PSGs are currently available as of September 2018
  - New PSGs are issued every quarter
  - More PSGs for complex products are under development

***Product-Specific Guidances for Generic Drug Development:***
*https://www.fda.gov/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm075207.htm*

# Pre-ANDA Program for Complex Products:
## 2. Guidance

| For NCE Products (non-complex) | For Complex Products | For Other Products |
|---|---|---|
| • FDA will issue PSGs for 90% of NCE NDAs approved on or after October 1, 2017, at least 2 years prior to the earliest lawful ANDA filing date | • There are Pre-ANDA meetings for complex products without a PSG or guidance<br>• FDA will strive to issue PSGs for complex products as soon as scientific recommendations are available | • Based on requests from the regulated industry and public health priorities |



NCE: New Chemical Entity; NDA: New Drug Application

# Pre-ANDA Program for Complex Products:
# 2. Guidance

## Timely PSGs to optimize ANDA reviews for all product categories

- Provide guidance to applicants early in development
- Coordination between guidance revisions and review
- Keep guidance up to date

## Timely PSGs to enable access to generics in all product categories

- Communicate research results
- Manage our pre-ANDA meeting capacity

# Product-Specific Guidance Drive Pre-ANDA Process

**Controlled Correspondence (Controls)**

- Questions on the guidance or PSG
- Complex product and alternative to guidance
  - Within the same study type

**Pre-ANDA Meetings**

- Complex product and no guidance
- Complex product and alternative to guidance
  - Different study type

# Pre-ANDA Program for Complex Products:
## 3. Pre-ANDA Meetings

- Pre-ANDA meetings accelerate access to generic complex products through early engagement with the FDA

- Three types of meetings:
  - Product development meetings
  - Pre-submission meetings
  - Mid-review cycle meetings

***Draft Guidance: Formal Meetings Between FDA and ANDA Applicants of Complex Products Under GDUFA:***
*https://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM578366.pdf*

# Pre-ANDA Program for Complex Products:
# 4. Controlled Correspondence (Controls)

## Standard Controls: 60 days

- Use for requests for information on a specific element of generic drug development (e.g., Q1/Q2)
- Or use for information on certain post-approval submission requirements

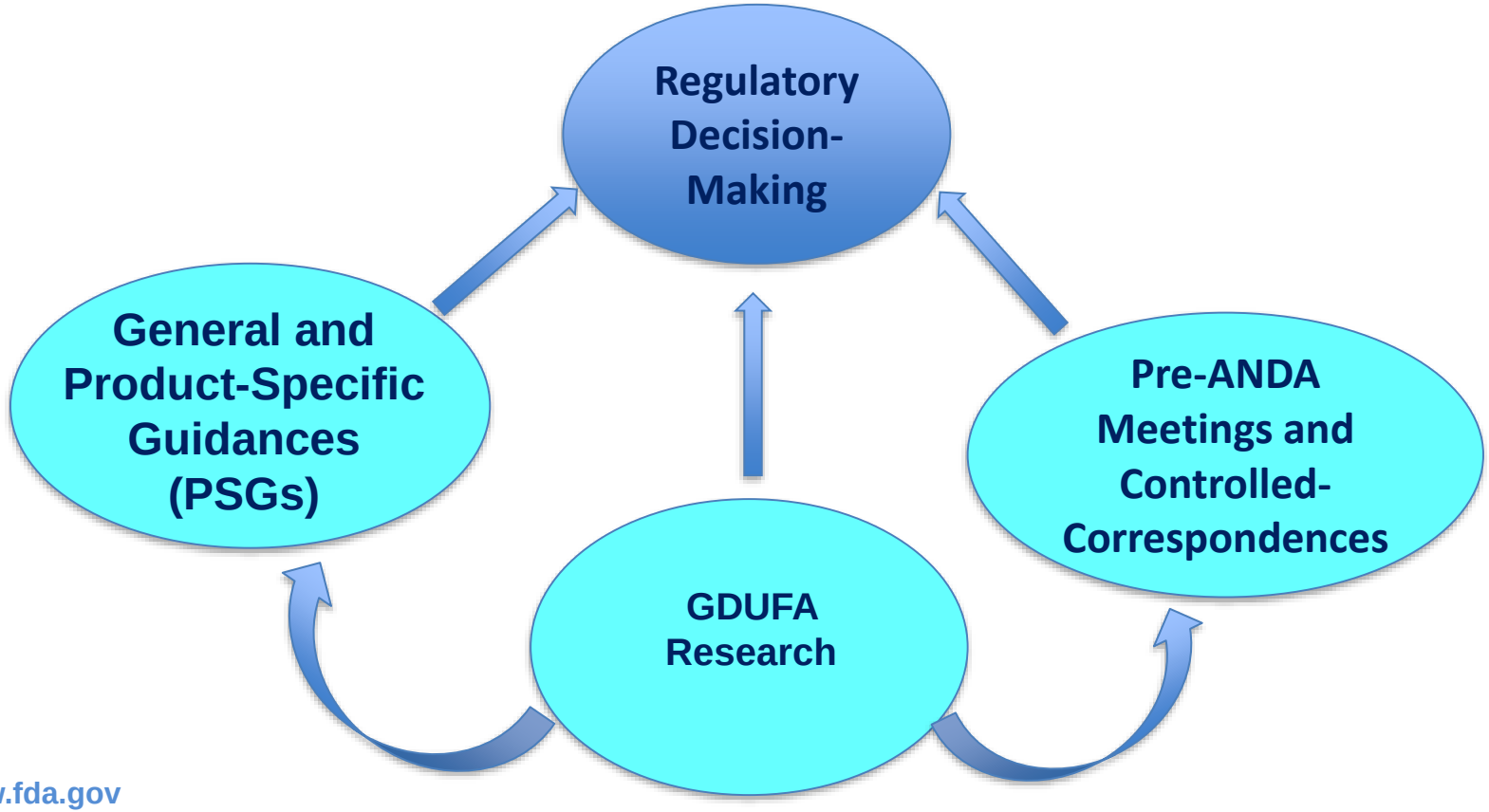
## Complex Controls: 120 days

- Evaluation of clinical content
- Review of protocols for drugs that reference-listed drugs with REMS ETASU
- Alternate BE within the same study type

REMS: Risk Evaluation and Mitigation Strategies; ETASU: Elements to Assure Safe Use

***Draft Guidance: Controlled Correspondence Related to Generic Drug Development:***
https://www.fda.gov/downloads/drugs/guidancecomplianceregulatoryinformation/guidances/ucm583436.pdf

# Science-Informed Regulatory Policy and Decision-Making



# Value Added:
# Pre-ANDA Program for Complex Products

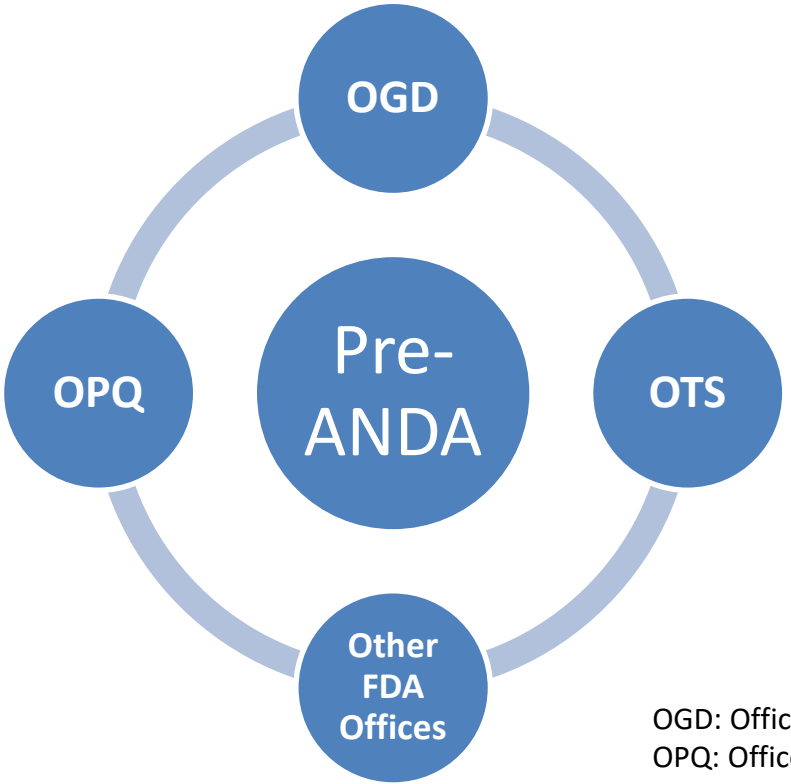
## Previously work often "back-loaded", e.g.,

- FDA did not issue PSGs far enough in advance due to workloads and resources
- Companies were unclear with regard to regulatory expectations, and they submitted ANDAs that missed key aspects
- FDA started grappling with the tough issues after ANDA was received
- Numerous review cycles and delay

## Now move to "Front Load", e.g.,

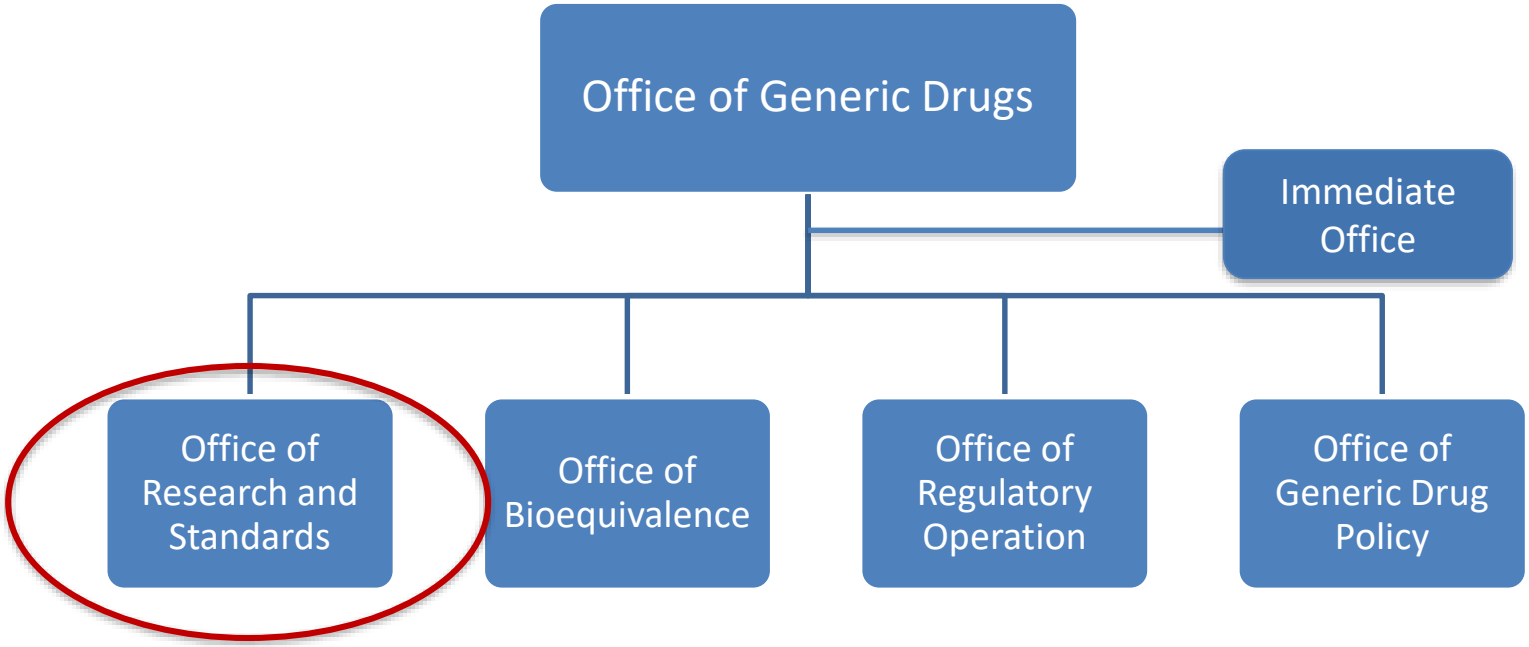
- Timely **PSGs** for both NCEs and Complex Products
- **Research** supports the pathways for generic product developments and standards recommendation for demonstrating therapeutic equivalence
- **Pre-ANDA meetings** to discuss issues and regulatory expectations
- Ensure high quality submissions and reduce review cycles

# Pre-ANDA Program
# Multi-disciplinary Engagement



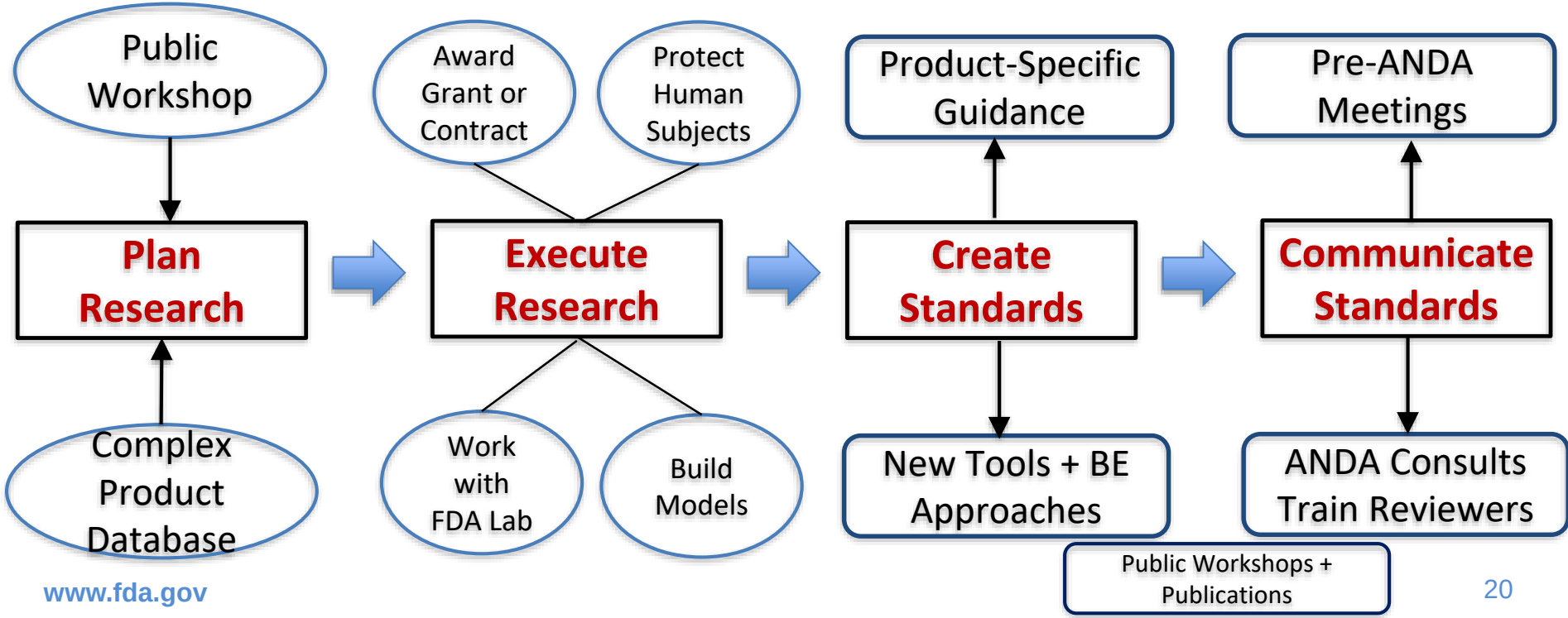

OGD: Office of Generic Drugs;
OPQ: Office of Product Quality
OTS: Office of Translational Sciences

# Office of Generic Drugs



# Office of Research and Standards

- ORS is a multidisciplinary **Office** in OGD that plans and conducts **Research** and translates the results into generic drug **Standards**



# Objectives of This Workshop

- Communicate how FDA research outcomes guide and facilitate complex generic product development
  - Link and leverage GDUFA science and research on complex products to product-specific guidance development
  - Discuss pre-ANDA meetings and review
  - Examine science related to complex products in various areas
- Provide a “deep-dive” to the complex generic drug development process
- Provide practical assistance to industry in submitting complete applications with a higher potential for first cycle approval

# Future Workshops/Meetings on Complex Generic Drug Products

- **FDA and DIA Co-sponsored Workshop: Complex Generic Drug-Device Combination Products**
  - October 9-10, 2018, Silver Spring, MD
- **Flight Simulator Workshop: Learning How to Develop Complex Generic Drug Products**
  - AAPS PharmSci 360: Pre-conference workshop
  - November 3, 2018, Washington DC
- **PBPK Modeling for the Development and Approval of Locally Acting Drug Products**
  - ASCPT Pre-Conference
  - March 13, 2019, Washington DC

# Acknowledgements


- Robert Lionberger
- Kris Andre
- Katherine Tyner
- Suneela Prodduturi
- OGD Policy and OGD Comms Staff
- Office of Research and Standards (ORS) Staff
- Other OGD offices
- OPQ and OTS


FDA
U.S. FOOD & DRUG
ADMINISTRATION