

Pre-ANDA Program Overview

Complex Generic Drug Product Development Workshop

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

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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

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

Pre-ANDA Program for Complex Products



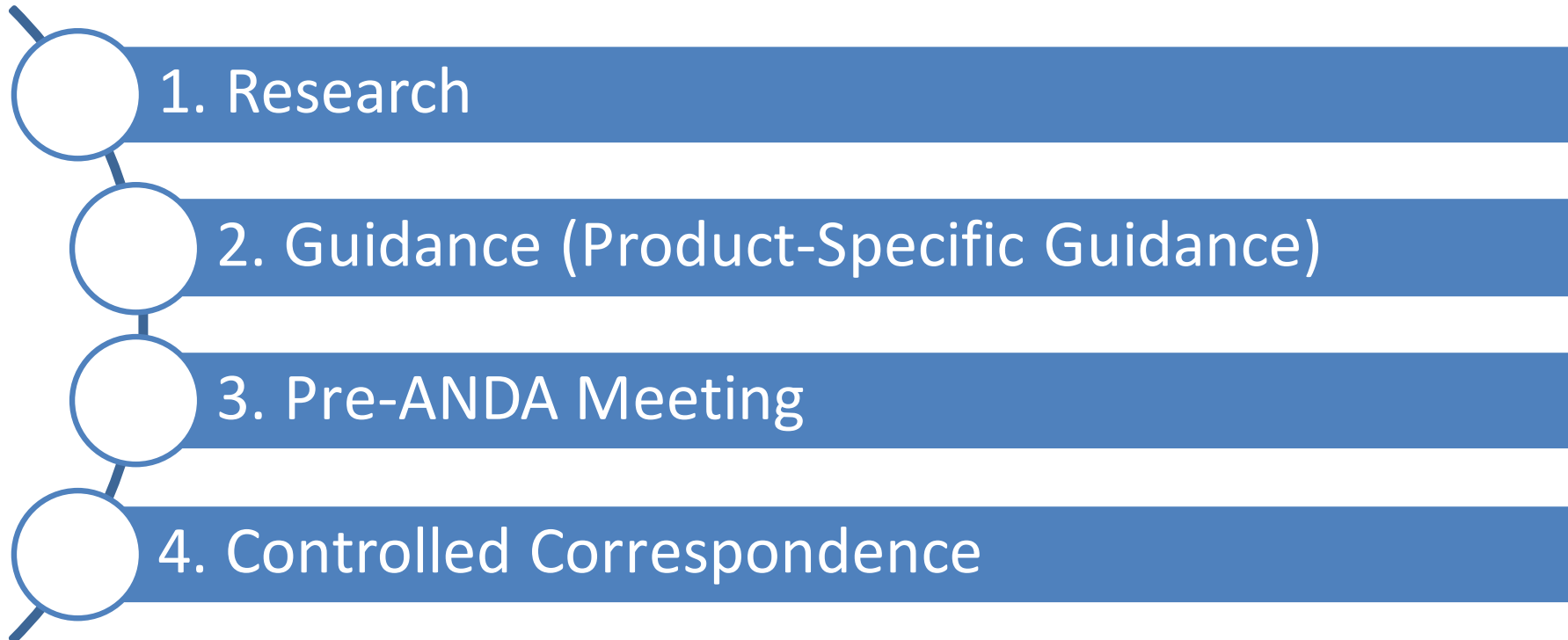
Goals of the Pre-ANDA Program Under GDUFA II



- 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

- 
- A vertical list of four steps, each represented by a white circle with a blue outline on the left, connected by a thin blue line. Each circle is positioned to the left of a horizontal blue bar that contains the text of the step.
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



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Generic Drugs

- Overview & Basics
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- Science & Research**
- Patient Education

Science & Research

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The Office of Research and Standards, a sub-office of the FDA Office of Generic Drugs, supports the regulatory science program established under the [Generic Drug User Fee Amendments \(GDUFA\)](#). In collaboration with industry and the public, FDA creates an annual list of regulatory science initiatives on generic drugs. The research studies conducted under these initiatives advance public health by providing access to safe and effective generic drugs. The results provide new tools for FDA to evaluate generic drug equivalence and for industry to efficiently develop new generic products.



Priorities & Projects

Learn more about FDA generic drug research priorities, public workshops, and awarded projects

Research Publications & Resources

Browse FDA generic drug research published in scholarly journal articles, presentations, and posters

Guidances & Reports

View FDA generic drug research publications, including product-specific guidances and annual reports

Collaboration Opportunities

See a listing of available grant and fellowship opportunities

Latest Science & Research News

- [Office of Generic Drugs FYs 2013 - 2017 Regulatory Science Research Report](#)
- [Public Workshop on May 24, 2018: FY 18 Generic Drug Research Public Workshop](#)
- [Nanotechnology Characterization Laboratory Unveils New Technical Services for Drug Developers](#) (3/9/18)

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



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

Pre-ANDA Program for Complex Products:

2. Guidance



For NCE Products (non-complex)

- 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

For Complex Products

- There are Pre-ANDA meetings for complex products without a PSG or guidance
- FDA will strive to issue PSGs for complex products as soon as scientific recommendations are available

For Other Products

- Based on requests from the regulated industry and public health priorities

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

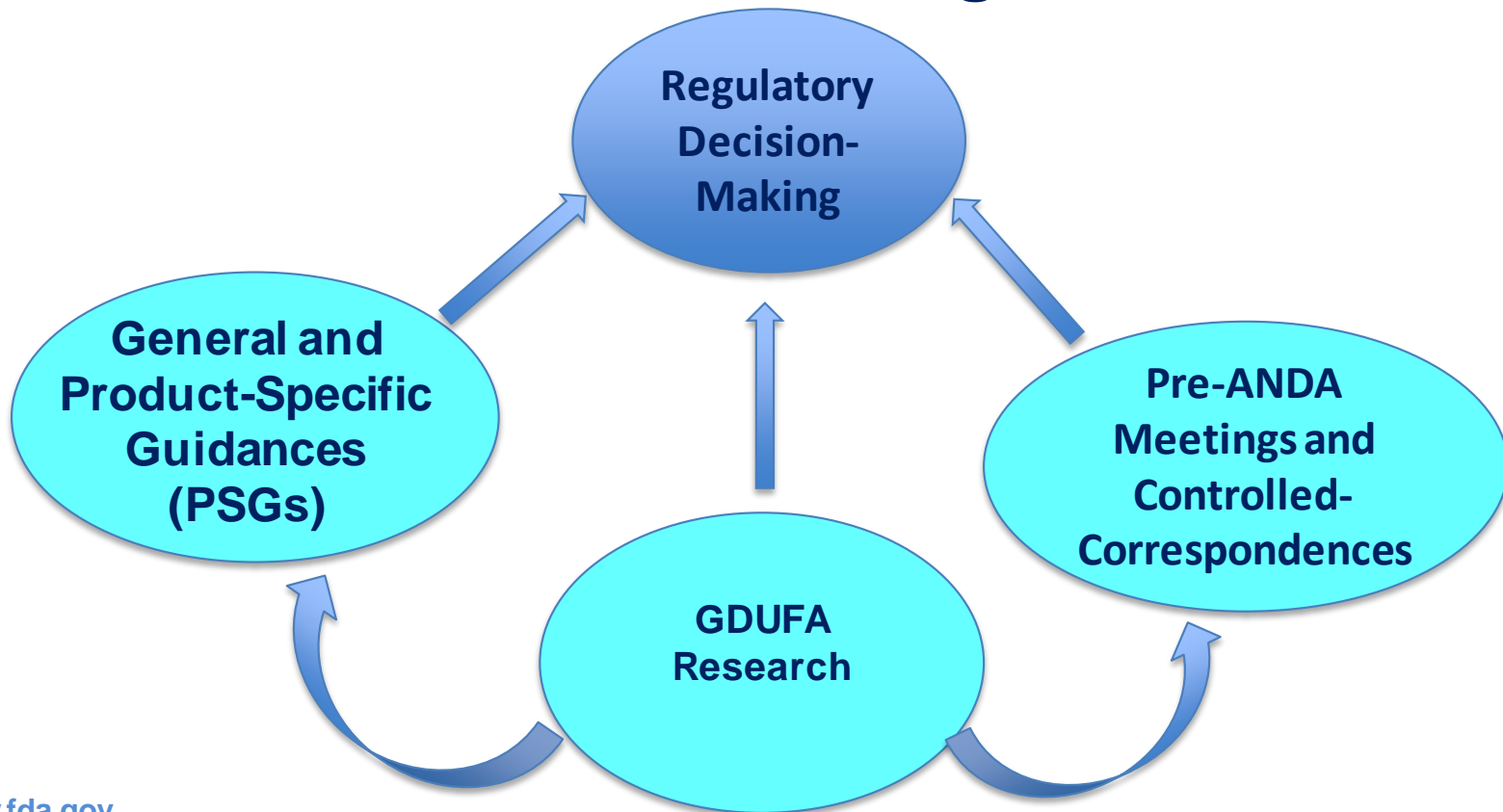
- Evaluation of clinical content
- Review of protocols for drugs that reference-listed drugs with REMS ETASU
- Alternate BE within the same study type

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.,

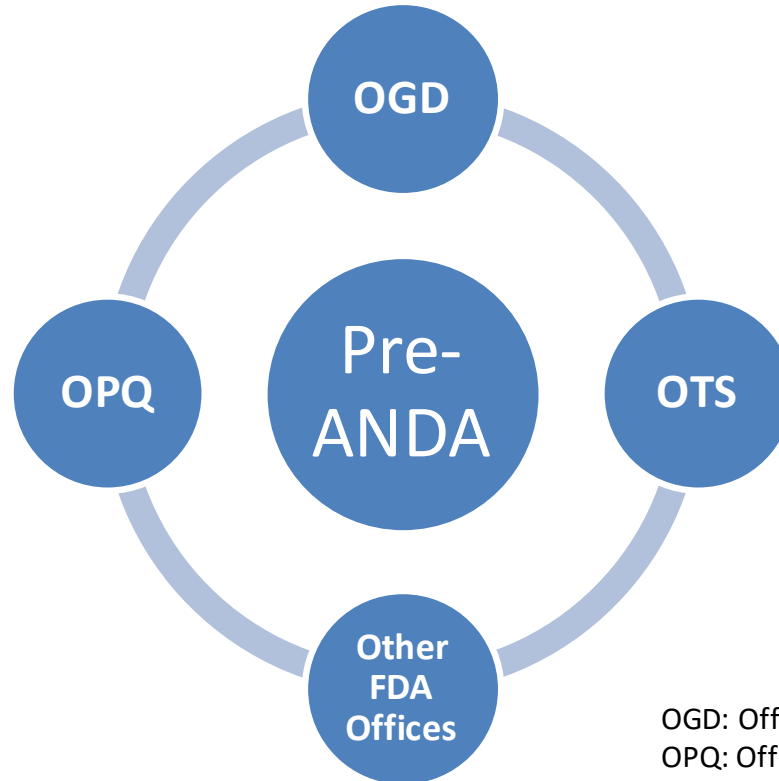
- FDA did not issue PSGs far enough in advance due to workloads and resources
- Companies were unclear with regard to regulatory expectations, and they submitted ANDAs that missed key aspects
- FDA started grappling with the tough issues after ANDA was received
- Numerous review cycles and delay



Now move to “Front Load”, e.g.,

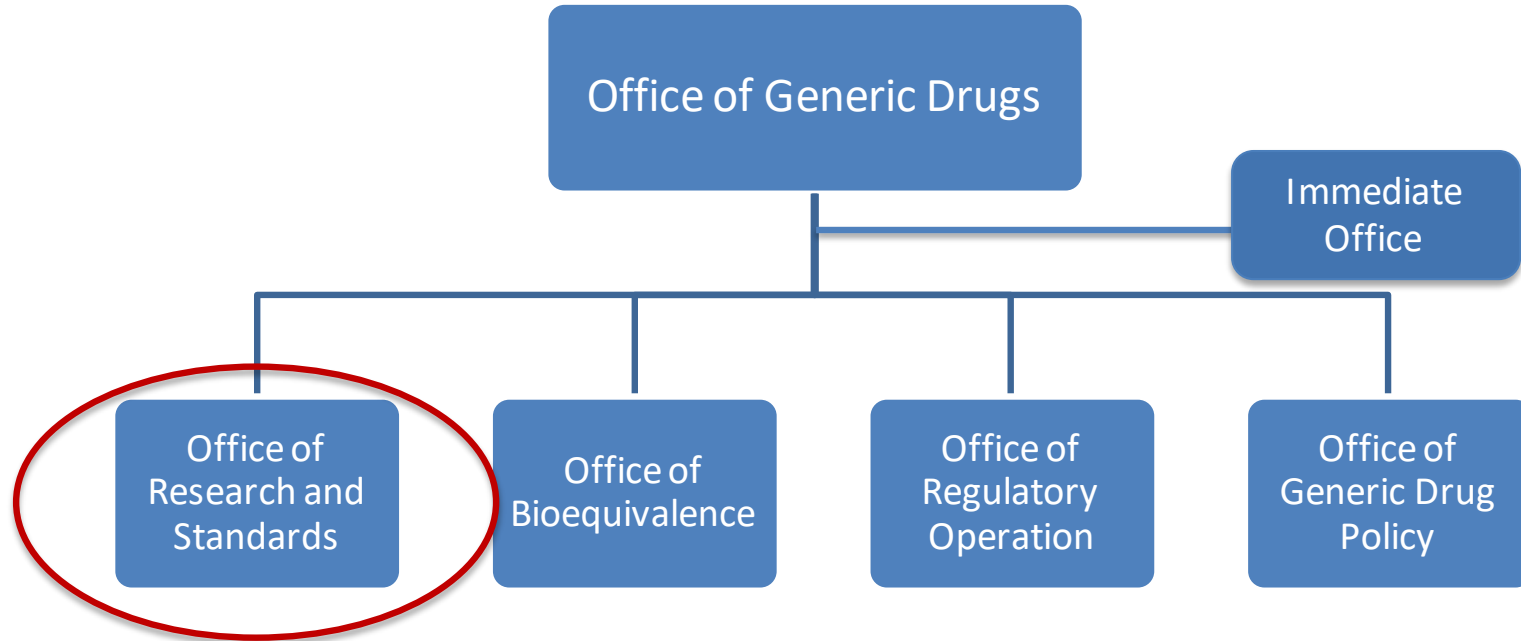
- Timely **PSGs** for both NCEs and Complex Products
- **Research** supports the pathways for generic product developments and standards recommendation for demonstrating therapeutic equivalence
- **Pre-ANDA meetings** to discuss issues and regulatory expectations
- Ensure high quality submissions and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

Pre-ANDA Program Multi-disciplinary Engagement



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

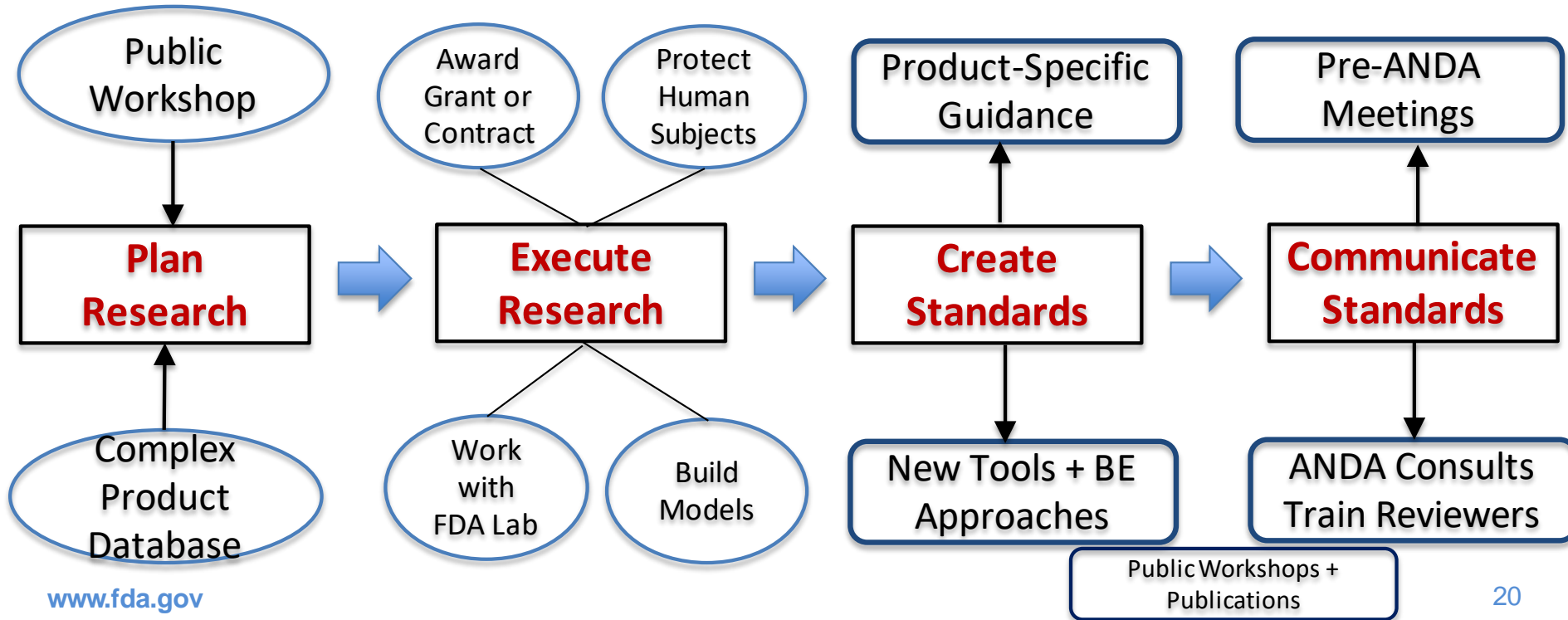
Office of Generic Drugs



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

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