U.S. FOOD & DRUG ADMINISTRATION

Complex Generics Town Hall

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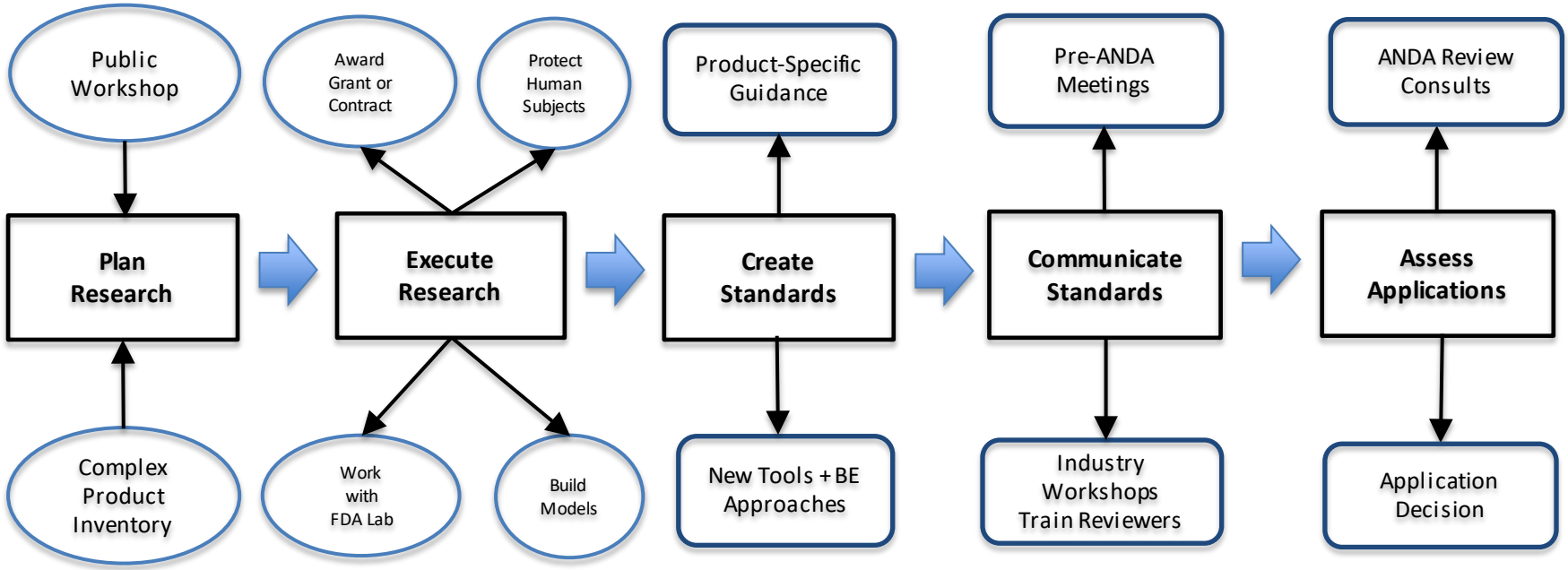
Integrated Pre-ANDA System Operational Model



ANDA: abbreviated new drug application

Scale of Research

- Stable investment supports internal and external research activities
  - >100 active projects
  - ~20 new grants or contracts/per year to leverage external expertise
- Input from industry via public meeting and FDA-Industry meetings helps direct focus of the research program

- Publications

FY	Publication (peer reviewed / presentation)
2017	46/97
2018	67/157
2019	79/133
2020	75/110
2021	64/97

- Workshops

FY	Workshops
2017	4
2018	8
2019	5
2020	5
2021	8

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GDUFA Science and Research Report

- The FY2020 GDUFA Science and Research Report is available at: https://www.fda.gov/drugs/generic-drugs/generic-drug-research-related-guidances-reports
- It highlights the scope and impact of **all** GDUFA-supported research across FDA
- High transparency to the generic industry on what we use GDUFA resources for

Unique Features of GDUFA Research

- Tight integration between research and scientific advice to generic applicants
  - Product-Specific Guidance
    - Written by staff doing research
  - Pre-ANDA Meetings
    - Led by staff doing research
- Focus on complex generics

Product-Specific Guidance (PSGs)

- ~1,922 PSGs are available
- FY 2021
  - 135 PSGs: 74 New, 61 Revised
    - 27 new PSGs and 26 revised PSGs for complex products
- FY 2020
  - 258 PSGs: 108 New, 150 Revised
    - 30 new PSGs and 94 revised PSGs for complex products
- FY 2019
  - 252 PSGs: 107 New, 145 Revised
    - 24 new PSGs and 117 revised PSGs for complex products
- FY 2018
  - 208 PSGs: 136 New, 71 Revised
    - 55 new PSGs and 19 revised PSGs for complex products
- FY 2017
  - 194 PSGs: 108 New, 86 Revised
    - 45 new PSGs and 43 revised PSGs for complex products

- Key Trends
  - Stable reliable quarterly postings because of GDUFA goals for non-complex new chemical entities (NCEs)
  - GDUFA II steady production of new PSG for complex products
  - FY2021 saw ~20 new or revised PSG that provided a more efficient BE approach
  - Topical Batch coming in FY2022!

Controlled Correspondences (CC)

- CC continue to increase
  - FY2021: 3,998
  - FY2020: 3,641
  - FY2019: 3,206
  - FY2018: 2,936
  - FY2017: 2,668
  - FY2016: 1,884
  - FY2015: 1,677
- Analysis
  - ~40% of controls are about complex products
  - ~7% of controls are "complex controls" with 120 day goal date
  - ~100 controls provided feedback on comparative analysis for combination products[7]

Pre-ANDA Meetings

- FY2020: 124 pre-ANDA meeting requests
- FY2020: 102 pre-ANDA meeting requests
- FY2019: 112 pre-ANDA meeting requests
- FY2018: 83 pre-ANDA meeting requests
- FY2017: 27 pre-ANDA meeting requests

- Use of the pre-ANDA meeting program continues to grow
- FDA has exceeded all GDUFA II goals related to pre-ANDA meetings
- Pre-ANDA meetings support innovation in BE approaches

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Complex ANDA Approvals

- Percent of Full ANDA approvals that are complex products
- FY2021: 13.2%
- FY2020: 13.0%
- FY2019: 12.7%
- FY2018: 12.5%
- FY2017: 12.0%

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- Complex generic share is growing
- ~25% of reference products are complex
- At parity, complex generic activity will be double what it is now

Complex ANDA Submissions

- Percent of ANDA submissions that are complex products
- FY2021: 16.9%
  - 14.5% had Pre-ANDA meeting
- FY2020: 15.3%
  - 16.5% had Pre-ANDA meeting
- FY2019: 13.3%
  - 8.6 % had Pre-ANDA meeting
- FY2018: 14.1%
  - 3.5% had Pre-ANDA meeting
- FY2017: 13.5%
  - 3.8% had Pre-ANDA meeting

- Complex generic share is growing
- Submissions are ahead of approvals
- ~25% of reference products are complex
- At parity, complex generic activity will be double what it is now
- ANDAs that used the pre-ANDA meeting process have quadrupled in GDUFA II

Research and Approval of ANDAs for Complex Products

- Dec 28, 2020: ANDA 208086 (Glucagon for injection)
  - First ANDA for a synthetic peptide with a rDNA origin Reference Listed Drug (RLD)
  - No ANDA approval without research on analytical and immunogenicity methods for peptide impurities
- Jan 15, 2021: ANDA 206604 (Ferumoxytol Injection)
  - First ANDA for parenteral iron in 10 years
  - No ANDA approval without research on characterization methods for complex injectables

Research and Approval of ANDAs for Complex Products

- Feb 26, 2021: ANDA 212450 Loteprednol Etabonate Ophthalmic Suspension
  - First generic ophthalmic suspension approved based on an in vitro BE approach
  - No ANDA approval without research on particle size measurement or ophthalmic absorption models
- March 1, 2021: ANDA 208269 Hydrocodone Bitartrate ER Tablets
  - First ANDA for an Abuse Deterrent opioid product
  - No ANDA approval without research on nasal insufflation PK studies and in vitro abuse deterrent evaluation

Center for Complex Generics

- FDA awarded a Center for Research on Complex Generics (CRCG)
  - Grant to the University of Maryland and the University of Michigan
  - http://www.complexgenerics.org/
- Enhance research collaborations with the generic industry to further the FDA's mission of increasing access to safe and effective generic medicines
  - Collaborative research, training, and exchange of resources
  - Two workshops in FY2021
  - Aggregated industry input for research prioritization
  - Focus on implementation of new approaches in ANDA submissions

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Parallel Scientific Advice (PSA) Pilot

- The pilot established a new PSA process for complex generic drugs (FDA)/hybrid products (EMA)
- Launched September 15, 2021
- The PSA General Principles document can be accessed via the "Global Generic Drug Affairs" website
  - https://www.fda.gov/drugs/generic-drugs/global-generic-drug-affairs

Overall Goals of PSA Pilot

- To provide a mechanism for EMA and FDA assessors to concurrently exchange with applicants their views on scientific issues during the development of complex generic drug/hybrid products
  - increase dialogue between the two agencies and applicants from the beginning of the lifecycle of a complex generic drug product
  - provide a deeper understanding of the basis of regulatory decisions
  - optimize product development
  - avoid unnecessary replication of studies or unnecessary diverse testing methodologies

Summary

- The Pre-ANDA system provides clarity and improves development efficiency
- For complex products, research provides an essential input to the pre-ANDA system
- Pre-ANDA interactions support innovative approaches to BE that can accelerate access to generics

Thanks!

- To the hundreds of staff across CDER in OGD, OPQ, and OTS/DARS, and other offices that contributed to the research, PSG and pre-ANDA meetings
- To the enumerable CDER staff who participated in the ANDA reviews of complex generics
- For more details
  - https://www.fda.gov/drugs/generic-drugs/science-research


This is not City Hall!

This is Town Hall!

Welcome to Town Hall!

- Town Hall is a community building
- ASK: Questions about the system for complex generics
- SHARE: Your experiences in developing complex generics and how we can improve the system
- BUILD: Help build an infrastructure that makes it more clear how to develop complex generics


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