U.S. FOOD & DRUG ADMINISTRATION

WELCOME

We will begin the GDUFA III public meeting promptly at 9:00 am ET

Tuesday, November 16, 2021

Welcome

Carter Beach, JD

Deputy Director

Office of Executive Programs, CDER

U.S. FOOD & DRUG ADMINISTRATION

Public Meeting on the Recommendations and Proposed Enhancements for Generic Drug User Fee Amendments Reauthorization (GDUFA III)

FY 2023 - FY 2027

Agenda

9:00 - 9:05 a.m. **Welcome**
Carter Beach
Deputy Director, Office of Executive Programs, Center for Drug Evaluation and Research (CDER), FDA

9:05 - 9:15 a.m. **Opening Remarks**
Jacqueline Corrigan-Curay,
Principal Deputy Director, CDER, FDA

9:15 - 9:30 a.m. **GDUFA II Successes**
Maryll Toufanian
Director, Office of Generic Drug Policy, Office of Generic Drugs, CDER, FDA

GDUFA III Proposals

9:30 - 10:15 a.m. **Advancing Approvals**

- Maximizing Each Review Cycle
- Improving Regulatory Communication
- Manufacturing and Facilities

10:15 - 10:30 a.m. **Break**

10:30 - 10:45 a.m. **Enhancing Approval of Complex Generics**

10:45 - 11:00 a.m. **Setting a Sound Financial Foundation**

11:00 - 11:15 a.m. **Industry Perspective**

11:15 - 12:00 p.m. **Stakeholder Presentations**

12:00 – 12:45 p.m. **Lunch**

12:45 - 1:50 p.m. **Public Comment Period**

1:50 - 2:00 p.m. **Closing Remarks**
Sally Choe
Director, Office of Generic Drugs, CDER, FDA

GDUFA III - Q & A

- You may ask clarifying questions in the Q&A field at the bottom of the screen throughout the meeting.
- If you have comments, please submit them to the public docket.

Opening Remarks

Jacqueline Corrigan-Curay, JD, MD

Principal Deputy Director

CDER

Background

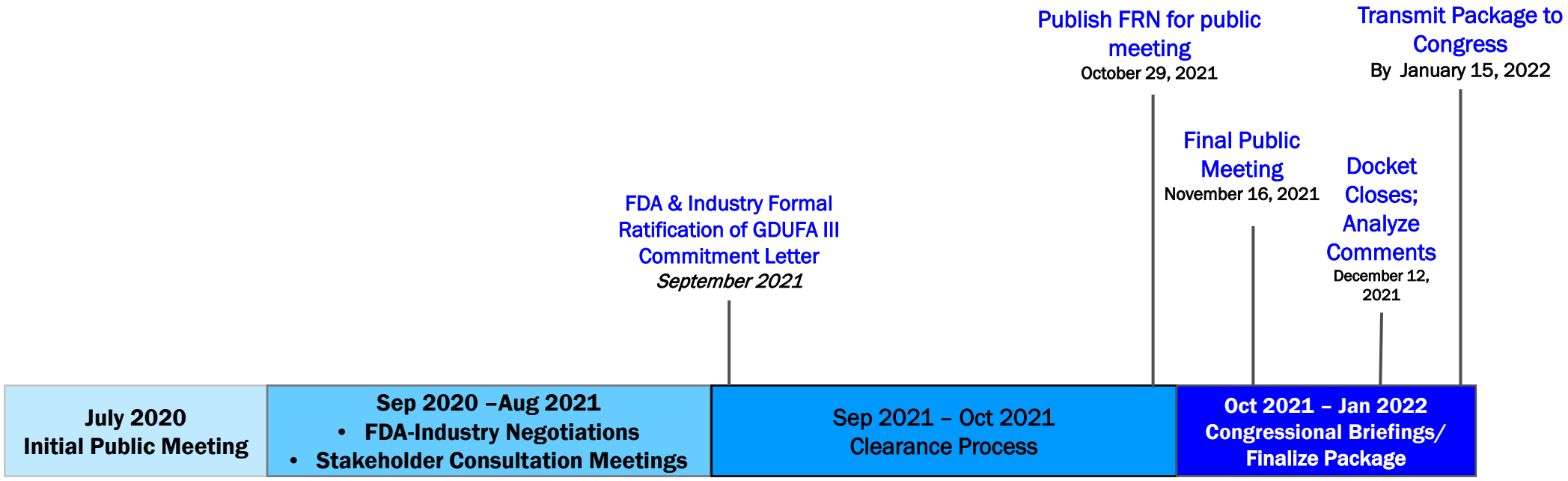
GDUFA I: FY 2013 – FY 2017

- FDA and industry's collective first effort to design a modern generic drug program
- First implementation of goal dates for ANDA submissions
- Make progress on the review of the ANDA backlog

GDUFA II: FY 2018 – FY 2022

- Improved and simplified goal date structure, especially for amendments
- Provided shortened goal dates for priority submissions
- Provided pre-ANDA program for complex products
- Provided accountability and reporting enhancements

GDUFA Reauthorization (GDUFA III) Targeted Timeline



GDUFA III Negotiation Objective:
- Maximize the Value of Each Review Cycle -

Discussions with industry representatives focused on the following areas identified by FDA, industry and public stakeholders:

- Advancing earlier cycle approvals through enhanced communication and review processes
- Enhancing the development, assessment, and approval of complex generic products
- Assuring a sound financial foundation for GDUFA III

Three industry trade groups at negotiations:

- AAM – Association for Accessible Medicines
- PBOA – Pharma & Biopharma Outsourcing Association
- BPTF – Bulk Pharmaceuticals Task Force

- Next Steps -

- Review the Federal Register (FR) notice and Commitment Letter
  - Available on FDA's Website https://www.fda.gov/drugs/news-events-human-drugs/public-meeting-reauthorization-generic-drug-user-fee-amendments-gdufa-11162021-11162021
- Public comments on FR notice due December 12, 2021
  - Docket No. FDA– 2020–N–1459 for ''Generic Drug User Fee Amendments; Public Meeting; Request for Comments" (https://www.regulations.gov/docket/FDA-2020-N-1459)
- FDA will review and analyze public comments on proposed recommendations
- Transmit final proposed package to Congress in January 2022

FDA GDUFA III Negotiators

Jacqueline Corrigan-Curay
Principal Deputy Center Director
FDA/CDER

Alonza Cruse
Director, Office of Pharmaceutical Quality Operations
FDA/ORA/OMPTO

Ashley Boam
Director, Office of Policy for Pharmaceutical Quality
FDA/CDER/OPQ

Maryll Toufanian
Director, Office of Generic Drug Policy
FDA/CDER/OGD

Edward "Ted" Sherwood
Director, Office of Regulatory Operations
FDA/CDER/OGD

Robert Lionberger
Director, Office of Research and Standards
FDA/CDER/OGD

Update on GDUFA II: Continued Success

Maryll Toufanian, JD

Director

Office of Generic Drug Policy, Office of Generic Drugs, CDER

Update on GDUFA II: Continued Success - Addressing Covid-19* -

- Approvals that expanded access to critical COVID-19 treatments:
  - 69 COVID-related original ANDAs
  - 1000+ COVID-related supplements
- Guidance
  - Development of ANDAs During the COVID-19 Pandemic – Questions and Answers
  - Protecting Participants in Bioequivalence Studies for ANDAs During the COVID-19 Public Health Emergency
  - Review Timelines for Applicant Responses to Complete Response Letters When a Facility Assessment Is Needed During the COVID-19 Public Health Emergency
- Public Presentations
  - COVID-19 Impact on Generic Drug Regulation and Evaluation
  - Addressing Common Challenges in Bioequivalence Studies Due to COVID-19

*As of October 15, 2021

Update on GDUFA II: Continued Success
- Increasing Generic Drug Access -

- GDUFA II successful in bringing all applications into a common goal date framework – truly "no application left behind"
- In FY 2021:
  - 670 + Approvals; 150 + Tentative Approvals
  - 90 + first generics
  - 1850 + Complete Response letters
  - 4700 + Information Requests and Discipline Review Letters
  - 550 + Drug Master File Reviews
- Milestone: 100 + cumulative Competitive Generic Therapy (CGT) approvals

Update on GDUFA II: Continued Success
- Notable Generic Drug Approvals in FY 2022 -

Generic Name	Brand Name	Indication	Approval Date
Glucagon for Injection packaged in an emergency kit	Glucagon for Injection packaged in an emergency kit	Severe hypoglycemia	12/28/2020
Linaclotide Capsules	Linzess Capsules	Irritable bowel syndrome with constipation and chronic idiopathic constipation	2/9/2021
Apremilast Tablets	Otezla Tablets	Moderate to severe plaque psoriasis	2/18/2021
Hydrocodone Bitartrate Extended-Release Tablets	Hysingla ER Tablets	Severe pain (Abuse Deterrent)	3/1/2021
Ibrutinib Capsules	Imbruvica Capsules	Mantle cell lymphoma (MCL)	3/31/2021
Enzalutamide Capsules	Xtandi Capsules	Prostate cancer	5/14/2021
Lenalidomide Capsules	Revlimid Capsules	Multiple myeloma, anemia, and certain lymphomas	5/21/2021
Tofacitinib Tablets	Xeljanz Tablets	Certain types of arthritis and ulcerative colitis	6/1/2021
Varenicline Tablets	Chantix Tablets	Smoking cessation	8/11/2021
Linagliptin Tablets	Tradjenta Tablets	Type 2 Diabetes Mellitus	8/31/2021

Update on GDUFA II: Continued Success
- Translating Science to Approval -

First complex generic of glucagon to treat severe hypoglycemia in patients with diabetes	• Approval of a synthetic peptide generic product was possible because of FDA research on analytical methods for peptides and immunogenicity testing for peptides.
First complex generic for a parenteral iron product that treats iron deficiency anemia	• FDA's scientific investment in characterization and advanced bioequivalence study designs was essential to this approval.
Complex generic for loteprednol etabonate ophthalmic suspension	• Investments in particle size characterization and eye models supported this more efficient in vitro bioequivalence method.

Update on GDUFA II: Continued Success
- FDA's Pre-ANDA Program -

- Reduce time from development to market
- Address complex scientific issues
- Communicate with prospective applicants
- Help applicants develop more complete submissions
- Clarify regulatory expectations

Update on GDUFA II: Continued Success
- The Center for Research on Complex Generics -

Update on GDUFA II: Continued Success
- Recent Workshops -

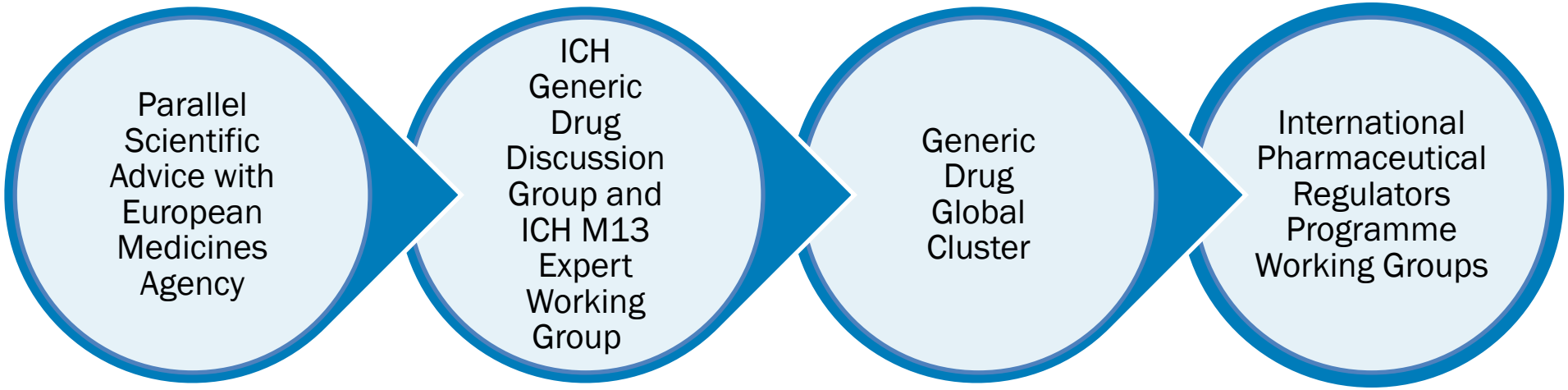
- Generic Drug Forum 2021: Lifecycle of a Generic Drug (April 2021)
  - Annual training for industry on how the generic drug program works
- Generic Drug Regulatory Science Initiatives Public Workshop (June 2021)
  - Annual workshop to obtain public input on research priorities
- In Vitro Release Test (IVRT) and In Vitro Permeation Test (IVPT) Methods: Best Practices and Scientific Considerations for ANDA Submissions (August 2021)
  - Scientific workshop hosted by the Center for Complex Generics
- Advancing Generic Drug Development: Translating Science to Approval (September 2021)
  - Scientific workshop focused on challenging issues during generic drug development
- Regulatory Utility of Mechanistic Modeling to Support Alternative BE Approaches (September 2021)
  - Scientific workshop hosted by the Center for Complex Generics

Update on GDUFA II: Continued Success
- Pre-ANDA Engagement -

- Enhanced research transparency and industry engagement
  - Bi-annual meeting with industry
  - Significant public outreach
  - Center for Complex Generics established
- Pre-ANDA meeting program established
  - Estimated 500 meeting requests
- Goal dates for Product Specific Guidance for New Chemical Entities established and met

Update on GDUFA II: Continued Success
- Global Engagement -

Proactive engagement on a number of international fronts:



Update on GDUFA II: Continued Success
- Maximizing Transparency: Final Guidances -

- *Referencing Approved Drug Products in ANDA Submissions,* Oct 2020
- *Formal Meetings Between FDA and ANDA Applicant of Complex Products Under GDUFA*, Nov 2020
- *Controlled Correspondence Related to Generic Drug Development*, Dec 2020
- *M9 Biopharmaceutics Classification System-Based Biowaivers*, May 2021
- *ANDAs for Certain Highly Purified Synthetic Peptide Drug Products That Refer to Listed Drugs of rDNA Origin Guidance for Industry*, May 2021
- *ICH Q12 Technical and Regulatory Considerations for Pharmaceutical Product Lifecycle Management,* May 2021
- *Development of Abbreviated New Drug Applications During the COVID-19 Pandemic – Questions and Answers*, Sept 2021

Update on GDUFA II: Continued Success
- Maximizing Transparency: Draft Guidances and MAPPs -

- Draft guidances:
  - *Bioequivalence Studies With Pharmacokinetic Endpoints for Drugs Submitted Under an Abbreviated New Drug Application*, August 2021
  - *Level II QA Controlled Correspondence*, September 2021
  - *Microbiological Quality Considerations in Non-sterile Drug Product Manufacturing.* September 2021

- MAPPs
  - MAPP 5240.5 Rev 2: ANDA Suitability Petitions, October 2020
  - MAPP 5230.3 Rev 1: Generic Drug Labeling Revisions Covered Under Section 505(j)(10) of the Federal Food, Drug, and Cosmetic Act, July 2021

Maximizing Each Review Cycle

Ashley Boam, MSBE
Director
Office of Policy for Pharmaceutical Quality, Office of Pharmaceutical Quality, CDER

Edward “Ted” Sherwood
Director
Office of Regulatory Operations, Office of Generic Drugs, CDER

Maryll Toufanian, JD
Director
Office of Generic Drug Policy, Office of Generic Drugs, CDER

GDUFA III Enhancements
- Maximizing Each Review Cycle -

- Pre-Submission Facility Correspondence (PFC)
  - Negotiated during GDUFA II to provide a pathway for an accelerated review of a priority application by allowing for presubmission of certain information on manufacturing facilities and bioequivalence studies to enable an assessment of the need for a pre-approval inspection
    - Provides sufficient time to schedule and perform the inspection within the shorter goal date
  - Increase industry's use of PFCs that enables priority ANDAs to receive an 8-month goal date by negotiation of the following changes:
    - Focus on the manufacturing information and bioequivalence study information that are critical for FDA to make an assessment regarding need for inspection
    - Non-substantial changes can be made to the information submitted in the PFC when the final bioequivalence study and manufacturing information comes in with the ANDA/Prior approval supplement (PAS) submission, provided it would not change FDA's assessment regarding the need for an inspection

GDUFA III Enhancements
- Maximizing Each Review Cycle (cont'd) -

- **Goal Date Extensions for Major Issues**
  - Mid-cycle Information Request (IR)/Discipline Review Letter (DRL) responses may trigger goal date extensions
  - Applies to first cycle amendments primarily from Quality and Bioequivalence disciplines
  - Extensions consistent with comparable standard or priority Major Amendment goals

- **Goal Date Extensions for Minor Issues**
  - IR/DRL responses may trigger goal date extensions
  - Applies to late first cycle and subsequent cycle amendments
  - Extensions consistent with comparable standard or priority Minor Amendment goals

GDUFA III Enhancements
- Maximizing Each Review Cycle (cont'd) -

- Imminent Action
  - In general, formalizes and standardizes GDUFA II “Imminent Approval” activity
  - Report on use of Imminent Actions

GDUFA III Enhancements
- Improving Regulatory Communication -

- Controlled Correspondence
  - Maintain the current process and goals
  - Replace terms standard and complex with level 1 and level 2
  - Allow Controlled Correspondence after an ANDA has been submitted in certain circumstances
    - Primarily after issuance of a Complete Response Letter or Tentative Approval
    - After ANDA approval
  - Respond to requests to clarify ambiguities within 21 days

GDUFA III Enhancements
- Improving Regulatory Communication (cont'd) -

- **Suitability petitions** – petitions from prospective applicants requesting permission to submit an ANDA for a different route of administration, strength, dosage form, or one different active ingredient in a fixed-combination drug product from a reference listed drug
- **Starting in FY 2024, goal dates** will be established for new suitability petitions
- In order to obtain a goal date, prospective applicants can withdraw a previous petition and resubmit
- In general, FDA will commit to addressing suitability petitions in the order that are received but will prioritize certain suitability petitions that:
  - could mitigate or resolve a drug shortage and prevent future shortages;
  - address a public health emergency declared by the Secretary of the U.S. Department of Health and Human Services under section 319 of the PHS Act, or anticipated under the same criteria as apply to such a declaration;
  - are for a new strength of a parenteral product that could aid in eliminating pharmaceutical waste or mitigating the number of vials needed per dose by addressing differences in patient weight, body size, or age; or
  - are subject to special review programs under the President's Emergency Plan for AIDS Relief (PEPFAR)

Manufacturing and Facilities

Ashley Boam, MSBE

Director

Office of Policy for Pharmaceutical Quality, Office of Pharmaceutical Quality, CDER

Alonza Cruse

Director

Office of Pharmaceutical Quality Operations, ORA

GDUFA III Enhancements
- Manufacturing and Facilities -

- **Type II Drug Master File* (DMF) Assessments**
  - DMFs remain a challenge for ANDA applicants because on average a DMF holder's response time to Agency questions exceeds 3 months, limiting ability for DMF to be adequate in one review cycle
  - GDUFA III will provide opportunities for early review of DMFs before priority ANDAs are submitted and between cycle review of solicited amendments to facilitate approvals

- **FDA Communication Related to DMF Amendments and ANDAs**
  - DMF amendments submitted late in the ANDA review cycle can lead to delays in approval or tentative approval of the ANDA
  - FDA will communicate to industry that prior to submitting a DMF amendment, the DMF holder should coordinate with the ANDA applicant that references the DMF to avoid such delays

* A Type II active pharmaceutical ingredient drug master file means a submission of information to the Secretary by a person that intends to authorize FDA to reference the information to support approval of a generic drug submission without the submitter having to disclose the information to the generic drug submission applicant. Section 744A(13) of the FD&C Act.

GDUFA III Enhancements
- Manufacturing and Facilities (cont'd) -

- Post-approval Questions from Applicants
  - GDUFA III will provide for expansion of controlled correspondence to include post-approval questions, which typically focus on manufacturing changes

- Facilities Ready for Inspection
  - If a facility named in an ANDA needs to be inspected preapproval to support the application, but is not "ready for inspection," this can lead to delays in approval or tentative approval.
  - GDUFA III will provide that an ANDA with a facility marked "not ready" on the Form FDA 356h will receive an extended goal date (15 months)
    - If the ANDA is amended to indicate that all facilities are ready during that initial period, FDA will set a new goal date from the date of that amendment.
    - If the ANDA is not amended indicating that all facilities are ready during that period, FDA will extend the goal date by another 15 months and will take action within the overall 30-month period.

GDUFA III Enhancements
- Manufacturing and Facilities (cont'd) -

- **Education regarding FDA surveillance inspections**
  - Providing information to foreign regulators regarding FDA's inspection procedures supports the export of safe and effective pharmaceutical products by the U.S.-based pharmaceutical industry
  - FDA will update the existing publicly available Inspection Classification Database webpage and will develop communication materials to provide further information to industry and foreign regulators on how FDA determines which facilities to select for a drug surveillance inspection, including how FDA uses its risk-based site selection model to determine the frequency of surveillance inspections

GDUFA III Enhancements
- Manufacturing and Facilities (cont'd) -

- Facilities
  - If a facility named in an ANDA has been found "official action indicated" (OAI) following a surveillance inspection, the ANDA cannot be approved.
  - New Post-Warning Letter Meeting will provide an opportunity for eligible facilities to meet with FDA after making progress on their corrective action plans in order to facilitate remediation of deficiencies.
  - A re-inspection is commonly needed to resolve the OAI status and allow related application approval and GDUFA III will include goals around timelines for both domestic and international facility re-inspections.

U.S. FOOD & DRUG ADMINISTRATION

Break

We will return promptly in **15 minutes**

Enhancing Approval of Complex Generics

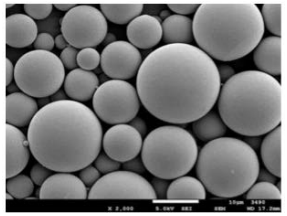
Robert Lionberger

Director

Office of Research and Standards, Office of Generic Drugs, CDER

GDUFA III Enhancements
- Definition of Complex Generic and Market Scope -

- **Remains the same as GDUFA II, e.g., :**
  - Locally acting (non-solution) products
  - Complex dosage forms
  - Product with a complex device constituent par
  - Product with complex active ingredients



Poly-lactic-co-glucolic Acid) (PLGA) microspheres

- **Scope of Market**
  - ~25% of active potential RLD
  - ~30% of active potential RLD without an approved generic
  - 13% of ANDA approvals

GDUFA III Enhancements
- Enhancing Approval of Complex Generics -

- Provide the regulatory science for new applications through new goal for completion of product specific guidances (PSGs) for complex products*
- Establish new teleconference/meeting when PSG impacts ongoing bioequivalence studies

* Adds to the commitment for PSGs for non-complex new chemical entity drug products (NCEs)

Enhance Communications around Review

- **Focus Pre-submission meetings** on key issues for review and assure review team participates
- Create option for more **enhanced scientific mid-cycle meeting** with goal of resolving more substantive issues within a single review cycle
- Establish **new post-CRL scientific meeting** to facilitate subsequent cycle approval

GDUFA III Enhancements
- Product Specific Guidance (PSG) -

- **GDUFA II PSG goals remain**
  - Provide PSG for non-complex NME 2 years after approval
  - Provide PSG for complex products as soon as possible
- **New goals for PSG for complex product new drug application (NDA) approved after 10/1/2022**
  - 50% in 2 years
  - 75% in 3 years

GDUFA III Enhancements
- Product Specific Guidance (PSG) (cont'd) -

- New commitment will provide additional resources and focus to ensure early availability of complex product PSG as new NDAs are approved
- FDA will continue the current level of effort on older complex products that do not have PSG available

GDUFA III Enhancements
- Value of PSG -

- Availability of PSG provides clarity on the path toward an ANDA submission
- PSG should not be restrictive of more efficient or innovative approaches to BE
  - Concern raised during negotiation
- PSG revisions may create uncertainty
  - In GDUFA II, FDA implemented notice of upcoming PSG revisions
    - Expanded and integrated into the GDUFA III commitment

GDUFA III Enhancements
- PSG Teleconference -

- If an applicant has begun an in vivo study that differs from the PSG recommendation
  - Eligible for a new t-con within 30 days of the request to discuss the potential impact of the PSG recommendation on the development program
  - Eligible for a new follow-up PSG meeting to address scientific issues or the justification for using an alternative to the PSG recommendation

GDUFA III Enhancements
- Pre-submission Meetings -

- **Significant revision in GDUFA III:**
  - Low uptake in GDUFA II (2-3 requested per year)
  - Perhaps because the 134-day timeline did not fit into the efficient movement toward submission

GDUFA III Enhancements
- Pre-submission Meetings (cont'd) -

- **New format in GDUFA III:**
  - Meeting within 60 days after the request
  - No questions from industry, focus on application orientation (what is unique)
  - FDA staff may provide feedback or advice
  - Eligibility is same as GDUFA II: If you have a PD meeting then you get the PS meeting

GDUFA III Enhancements
- Value of Pre-submission Meetings -

- Intended value creation
  - Form ANDA review team when the meeting request comes in
    - Allow internal knowledge transfer
    - Give more prep time for unique or complex issues
    - Support a more efficient ANDA review
- Will only be effective if industry uses this option

GDUFA III Enhancements
- Mid-cycle Meeting -

- Improvements in GDUFA III:
  - Eligibility is the same as GDUFA II => Complex product that had a pre-ANDA meeting
  - Within 7 days of the last mid-cycle communication, an eligible applicant may request one of two mid-cycle meetings. The request should describe the specific deficiency(ies) to be discussed.

    - A mid-cycle meeting,
      - Held within 30 days of the request
      - An applicant may ask for the rationale for any deficiency identified in the mid-cycle DRL(s), and/or questions related to FDA's assessment of the data or information in the ANDA

      OR

    - An enhanced mid-cycle meeting with a 60-day goal date extension
      - Held within 90 days of the last mid-cycle DRL
      - An applicant may ask questions about potential new data or information to address any possible deficiencies identified in the mid-cycle DRL(s).

GDUFA III Enhancements
- Value of Mid-cycle Meeting -

- Revision will allow more interaction at the mid-cycle meeting
  - Both options require applicant to develop questions
- Allows applicant to optimize the review process
  - More effort in the current cycle OR
  - Move quickly to final decision on the cycle

GDUFA III Enhancements
- Post-CR Scientific Meeting -

- New feature of GDUFA III for complex products
- Discuss a new equivalence study or approach that is different from that submitted in the ANDA
  - a change in study type from in vivo to in vitro
  - a new comparative use human factors study
  - a new approach to demonstrating sameness of a complex active ingredient

GDUFA III Enhancements
- Post-CR Scientific Meeting (cont'd) -

- Scientific discussion beyond the scope of the new controlled correspondence process
- Similar to the product development meeting (discuss complex scientific issues)
- FDA will grant or deny within 14 days and hold the meeting within 90 days after the decision

GDUFA III Enhancements
- Value of Post-CR Scientific Meeting -

- Product Development Meetings are very successful but can not be used post-submission
- Help resolve complex scientific issues that are blocking the path to approval

GDUFA III Enhancements
- GDUFA Progress on Complex Generics -

- GDUFA I added a research program that advances the science for complex generics
- GDUFA II added a pre-ANDA meeting program to improve scientific advice during development
- GDUFA III adds post-submission enhancements to help move complex products toward approval

GDUFA III Finance: Setting a Sound Foundation

Lisa Berry

Division Director

Division of User Fee Management, Office of Management, CDER

Bethany Rue

Data Scientist

Resource Capacity Planning, Office of Program and Strategic Analysis, Office of Strategic Programs, CDER

GDUFA III Finance
- Overview & Enhancements -

What's new for GDUFA III:

- Fee Structure Changes
- Additional Resources to Hire Staff
- Annual Capacity Planning Adjustment (CPA)
- Annual Operating Reserve Adjustment (ORA)

GDUFA III Finance
- Fee Structure: Revisions to allocation among fee types -

Allocation of Fee Revenue among Fee Types			
GDUFA II		**GDUFA III (Proposed)**	
ANDA Filing Fee	33%	*No Change*	33%
ANDA Program Fee	35%	↑	36%
DMF Fee	5%	*No Change*	5%
API Facility Fee	7%	↓	6%
Generic Drug Facility Fee (FDF)	20%	*No Change*	20%
CMO: % of FDF fee	33.3%	↓ CMO: % of FDF fee	24%
Foreign API and Generic Drug (FDF) Facilities continue to pay the $15,000 Foreign Facility Fee Differential			

GDUFA III Finance
- Hiring & Financial Transparency -

- Additional Resources
  - 128 staff to be hired in FY 2023 for the generic drug program
  - Confirm progress in the hiring of GDUFA III staff in the GDUFA 5-year financial plan
- Financial Transparency
  - Continue the GDUFA II commitments of publishing a 5-year financial plan and holding a public meeting to discuss the plan and other financial commitments every fiscal year

GDUFA III Finance
- Resource Capacity Planning & Capacity Planning Adjustment –

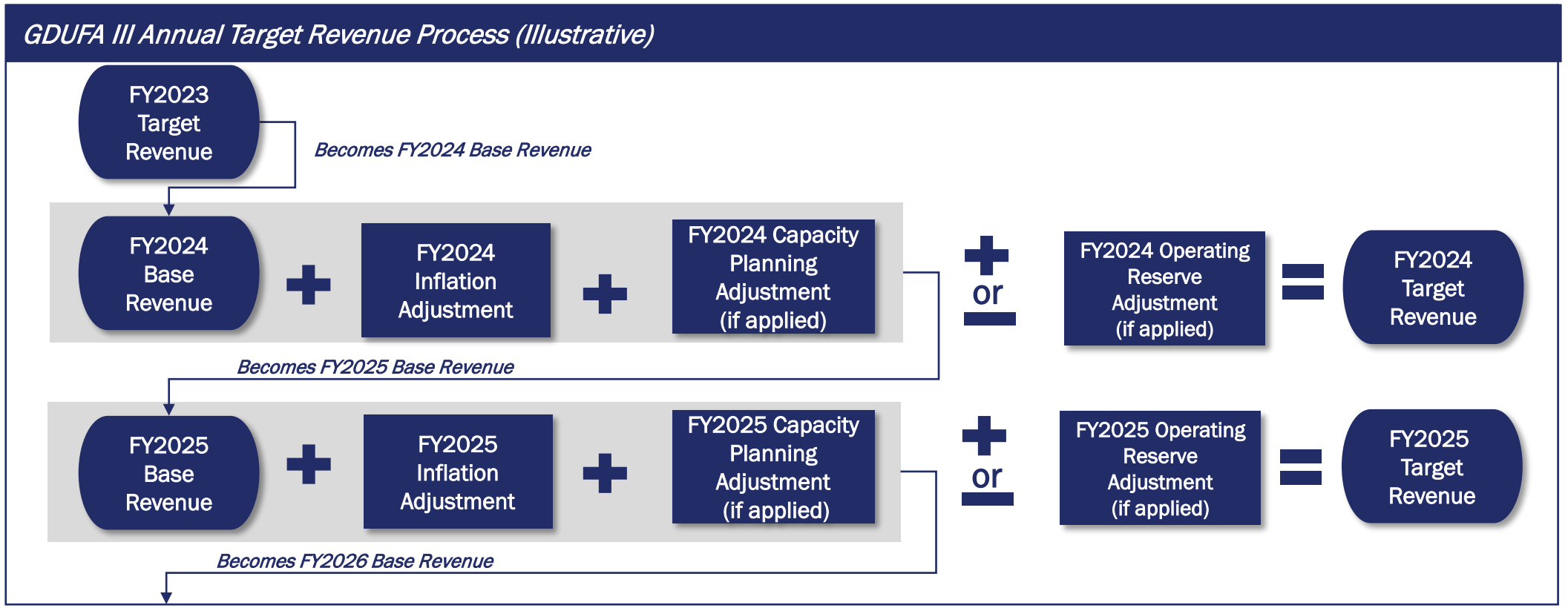
- **Resource Capacity Planning (RCP)**
  - Continues activities to mature the RCP capability, including: 1) Publish a plan outlining the implementation of the CPA and integration of RCP analyses in the Agency's resource and operational decision-making processes; 2) Conduct 3rd party evaluation of the RCP capability and CPA by end of FY 2025.
- **Capacity Planning Adjustment (CPA)**
  - Methodology to annually adjust target revenue for the additional resource needs due to sustained increases in workload for the GDUFA program.
  - First year of implementation for **FY 2024**.
  - Adjusts for sustained workload driven by direct review work*
  - Cap at 3 percent of annual inflation-adjusted target revenue unless certain conditions are met.

* Note direct review work considered to be: ANDA Originals and Resubmissions/Amendments; ANDA Supplements (PAS and CBE) and Amendments; Controlled Correspondences as defined in GDUFA III (see slide 28); Pre-ANDA Meetings (Pre-submission, Pre-submission PSG (see slide 42), and Product Development); Surveillance Inspections; Post-marketing Safety activities; and Suitability Petitions (see slide 29)

GDUFA III Finance
- Operating Reserve Adjustment -

- **Operating Reserve Adjustment**
  - Starting in FY 2024, optional annual adjustment of up to 8-10 weeks of operating reserve phased in from between FY 2024 and FY 2026.
    - GDUFA will continue to have flexibility rather than a set required amount.
    - Target revenue decreased if projected operating reserves exceeds 12 weeks.
    - Final Year Adjustment eliminated.

GDUFA III Finance
- Annual Target Revenue Process -



Industry Perspective

Industry Perspective

Lisa Parks

Vice President, Sciences and Regulatory Affairs

Association for Accessible Medicines (AAM)

Stakeholder Comments

Stakeholder Comments

Tonya Winders

President and CEO, Allergy & Asthma Network

President, Global Allergy & Airways Patient Platform

U.S. FOOD & DRUG ADMINISTRATION

Lunch

We will return promptly in 45 minutes

Public Comments

Public Comments

Molly Ventrelli

Senior Vice President, Regulatory Affairs

Fresenius Kabi

Public Comments

Kiran Krishnan

Senior Vice President, Global Regulatory Affairs

Apotex

Public Comments

Diana Zuckerman

President

National Center for Health Research

NATIONAL CENTER FOR HEALTH RESEARCH
The Voice For Prevention, Treatment And Policy

GDUFA: Safety Metrics

November 16, 2021

Diana Zuckerman, PhD, President

National Center for Health Research

#PatientNetwork

Disclosures

The National Center for Health Research is a nonprofit think tank that focuses on the safety and effectiveness of medical and consumer products and does not accept funding from companies that make those products.

#PatientNetwork

Metrics in the Commitment Letter

#6: Number of inspections conducted by domestic or foreign establishment location and inspection type (preapproval inspection, surveillance, bioequivalence clinical and bioequivalence analytical) and facility type (finished dosage form, API);

7: Median time from beginning of inspection to Form FDA 483 issuance;

Metrics in the Commitment Letter (cont'd)

8: Median time from Form FDA 483 issuance to Warning Letter, Import Alert and Regulatory Meeting for inspections with final classification of "Official Action Indicated" (or equivalent),

#9: Median time from date of Warning Letter, Import Alert or Regulatory Meeting to resolution of the "Official Action Indicated" status (or equivalent);

Metrics in the Commitment Letter (cont'd)

#12: Number of citizen petitions to determine whether a listed drug has been voluntarily withdrawn from sale for reasons of safety or effectiveness pending a substantive response for more than 270 days from the date of receipt;

#18: Percentage of facility re-inspections carried out within 4 or 8 months after the letter to the facility indicating FDA's intent to reinspect for domestic or foreign facilities, respectively;

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Public Comments

Brian McCormick

Vice President & Chief Regulatory Counsel, Head of Global Regulatory Policy

Teva Pharmaceutical Industries Ltd.

Public Comments

Raghuram Pannala

Vice President, CQC, PV, RA

ScieGen Pharmaceuticals, Inc.

Public Meeting on the Reauthorization of Generic Drug User Fee Amendments (GDUFA III)

Dr. Raghuram Pannala
Vice President-CQC, PV & RA
ScieGen Pharmaceuticals Inc.,

NOVEMBER 16, 2021

Disclaimer

ScieGen Pharmaceuticals appreciates the efforts from FDA leadership and all the scientific staff involved in the journey and learning curve of pre-GDUFA, GDUFA I and GDUFA II.

The suggestions presented are proposals only.

The case study presented is a sole case as an example and to analyze the opportunity for betterment. There are many ANDAs for which approval was received in quick turn around time [10 -14 months].

GDUFA Fees

Filing Fees
[DMF, ANDA]

- Initial review
- Life cycle management

1

Program Fees

- Scientific enhancement
- Complex generics

2

Facility Fees

- Audits
- Novel techniques, ET
- Continuous manufacturing

3

Initial review and Life cycle management

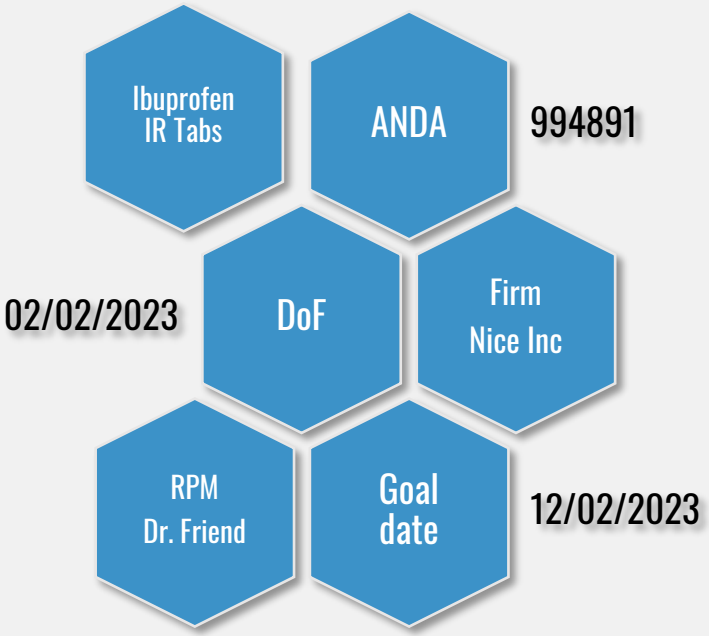
Tracking of an ANDA in real time like in e-commerce or other few government agencies to be made possible.

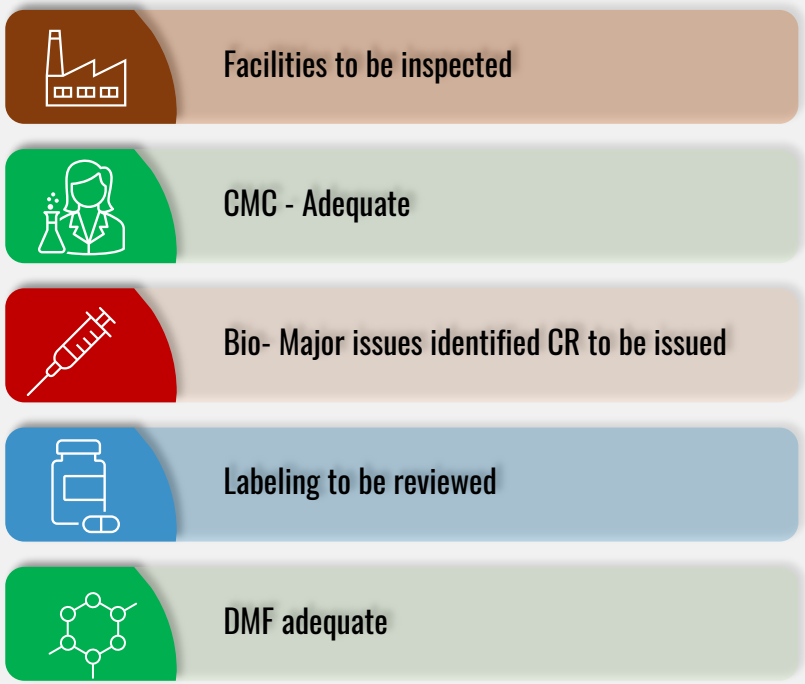
Predicted approvability should be displayed along with review status and next communication or correspondence.

May be linked to CDER NextGen or any other secured login.

Example snapshot….

Application Track Dashboard





CASE STUDY – ANDA Review

Last moment Dissolution method change as per deficiency, Labeling Revision due to dissolution method change and unsolicited DMF amendment that did not affect the ANDA sections led to extended ANDA goal date.

ANDA# XXX Tablets filed under GDUFA – II		
Filing Date	Feb- 2018	
Goal date	Dec- 2018	
DRL-Quality	Aug- 2018 [Dissolution spec proposed by agency not agreed by firm]	
Minor-CR	Dec- 2018 (Response submitted in Dec -2018)	May have been avoided if firm has agreed the specs
Revised Goal date	Jan -2019	
DMF Amendment filed	Feb -2019 [DMF amendment not effecting ANDA quality sections]	May have been avoided if agency has issued the DMF deficiency earlier
Revised Goal date	May -2019	
Minor-CR	May -2019 (Agency recommended to revise labeling to represent revised dissolution method and specifications)	This could have been issued along with the minor CR (Dec-2018) on dissolution
Approval Date	Aug - 2019	
Duration to receive final approval from the date of filing	20 months	

Initial review

Major review points, facility inspections status and DMF deficiencies to be communicated to industry during first IR communication.

Automated mid cycle review status communications including each discipline status update.

Quarterly/ periodical reports on top 10 deficiencies in ANDAs & DMFs.

Administrative forms revisions to be informed through FDA emails [version changes 356h, filed alert form, DMF 3938 form].

Aligning PET and regulatory clearance teams at an appropriate time to avoid last minute delays.

- Quick communications related to DMF amendments delaying final goal date of ANDA.
- Expanding controlled correspondence guidance scope to cover wide array of activities. [Recent CC Q&A guidance is appreciated].
- Priority ANDAs granted under MAPP 5240.3 with 10 months goal date only. No other advantage for listing as priority ANDA under MAPP 5240.3.
- During ANDA review, If RLD labeling is approved with new efficacy study or indications then agency model labels with carve out exclusivities may be issued to industry ASAP.

Life Cycle Management

FDA is embracing ET, continuous manufacturing and novel technologies at the same time it will be highly appreciated if guidance help is offered to aging facilities in terms of maintenance, old technologies switching to new technologies and changes.

Example	Expectations
▪ A firm wants to implement continuous manufacturing – for some it is CBE-30 change. ▪ A firm want to switch from tray drier to FBD – PAS change [a robust old molecule with proven data]	Revising Changes to NDA and ANDA (Issued: 2004) and SUPAC-IR CMC, In-vitro Dissolution and In-vivo Bioequivalence guidance (Issued: 1995), SUPAC-IR Q&A (Issued: 1997), SUPAC-Manufacturing Equipment Addendum (Issued: 2014) in line with current scenarios.

a) Drug product
   - Dry to wet granulation or vice versa.
   - Change from one type of drying process to another (e.g., oven tray, fluid bed, microwave).

b) Drug substance
   - Filtration to centrifugation or vice versa.

DMF Initial review and Life cycle management

Allowing DMFs to file amendments independently as CBE-0, CBE-30.

Facilitate Certain DMF updates as annual reportable like stability data, additional manufacturing blocks, simple analytical changes, intermediate & starting material changes that are not affecting ANDA.

Hidden facilities to be communicated to ANDA holder in 30 days. [thanks to form 3938]

- Starting material redesignation should be covered under DMF first assessment comments and it should be completed before listing under 'DMF List available for reference'.
- DMF reviews which are not affecting any sections of ANDA near TAD leads to missing approvals.

Scientific enhancements

It would be helpful if model documents, or templates are released for some critical documents. [thanks for QbD and Labeling QbR models]

- Nitrosamine risk assessment model [ICH provided ICH Q3D model reports for implementation].
- Annual report model.
- Impurity profile section in DMF and ANDA.
- 'Established conditions proposal' model for each dosage form.

- Update on Quality metrics program.
- SBIA workshops and training programs are helpful and helping a lot.
- *** SBIA workshops and case studies presented in Drug Master File (DMF) and Drug Substance (March 2021), Advancing Generic Drug Development: Translating Science to Approval , FY 2021 Generic Drug Science and Research Initiatives Public Workshop are very useful the efforts and content are appreciated.

Facilities & Inspections

Thanks for all the developments mentioned in GDUFA III commitment letter [Facilities and CPA]

Facility inspection status database should be updated with most recent data

OAI classification – inspections may be finished quickly compared to Warning letter

Transparency on how FDA select Risk based inspections to predict ANDA approvals.

Inspection Classification Database and Search

- To search for inspections, use the FDA Data Dashboard.
- New!! Inspection Classification from 10/1/2008 through 10/14/2021 (Report Date - October 2021) (Excel Format) ** This dataset will be decommissioned in January 2022. Inspection Classification data can be found on the FDA Data Dashboard.

Acknowledgements

- FDA
- ScieGen management
- Colleagues

Thank You!

GDUFA III - Q & A

- You may ask clarifying questions in the Q&A field at the bottom of the screen throughout the meeting.
- If you have comments, please submit them to the public docket.

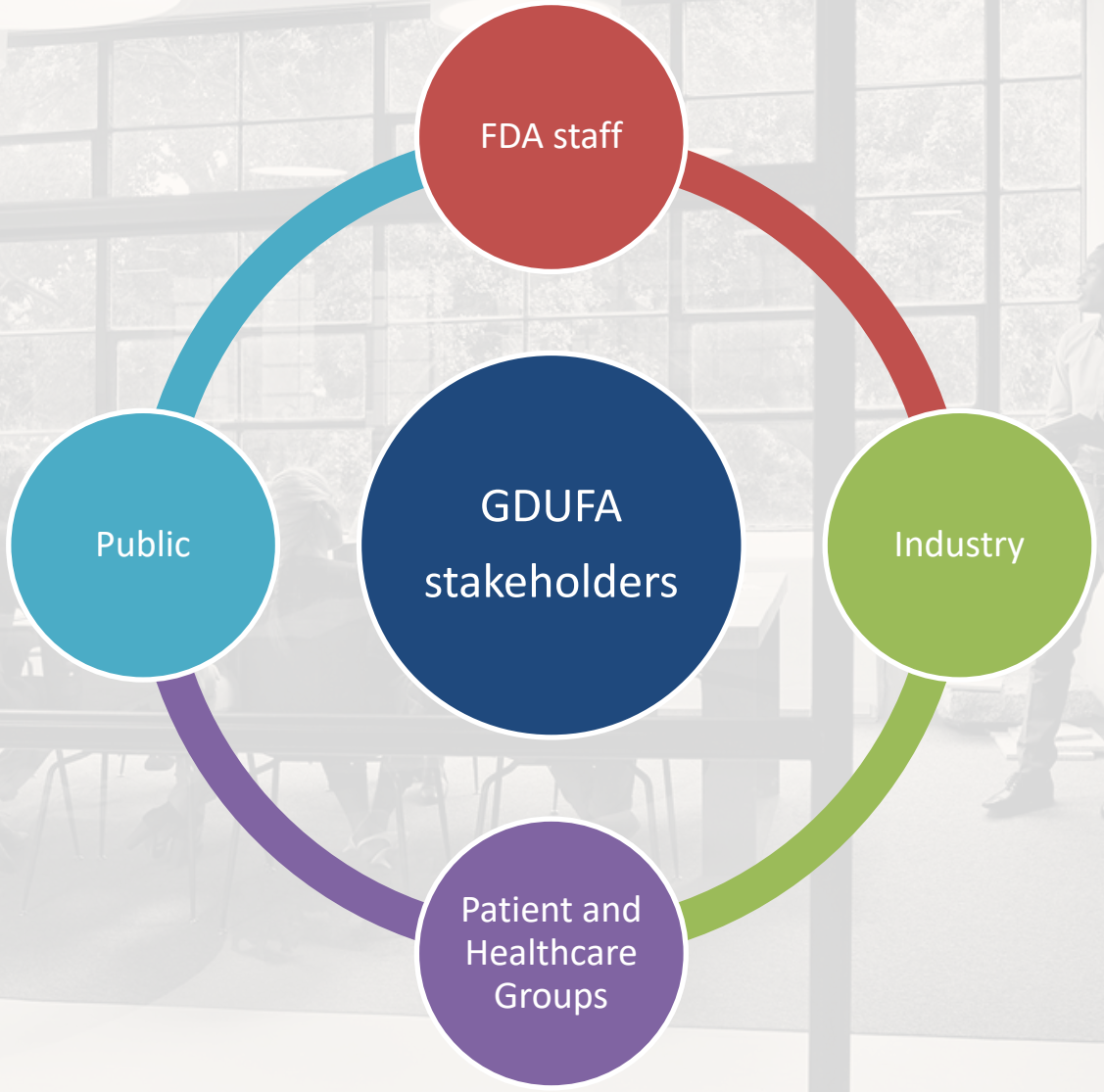
Closing Remarks

Sally Choe, PhD

Director

Office of Generic Drugs, CDER

Thank You


FDA staff
Public
GDUFA stakeholders
Industry
Patient and Healthcare Groups

The Next Era: GDUFA III

- Advance earlier approvals
- Enhance development, assessment, approval of complex generics
- Assure sound financial foundation

Steps Toward Implementation

Review public comments → Transmit recommendations to Congress → Congressional enactment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