Office of Generic Drugs Director's Update –

"LIFE WITH GDUFA"

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Disclaimer

- This presentation reflects the views of the speaker and do not reflect official FDA, HHS, or other government opinion or policy.
- I have nothing to disclose.

GOALS

Provide updates:

1. GDUFA
   - Review commitments
   - Changes induced by GDUFA
   - Accomplishments
2. Office of Generic Drugs (OGD)

GDUFA

- Increased:
  - Responsibility
  - Obligations
  - Commitments
  - Accountability
  - Quality
    - Applications, responses, communication
    - “Efficiency enhancements”

- For FDA **and** industry

GDUFA was/<u>is</u> a major GAMECHANGER

TRANSFORMATIONAL CHANGE

GDUFA = GAMECHANGER

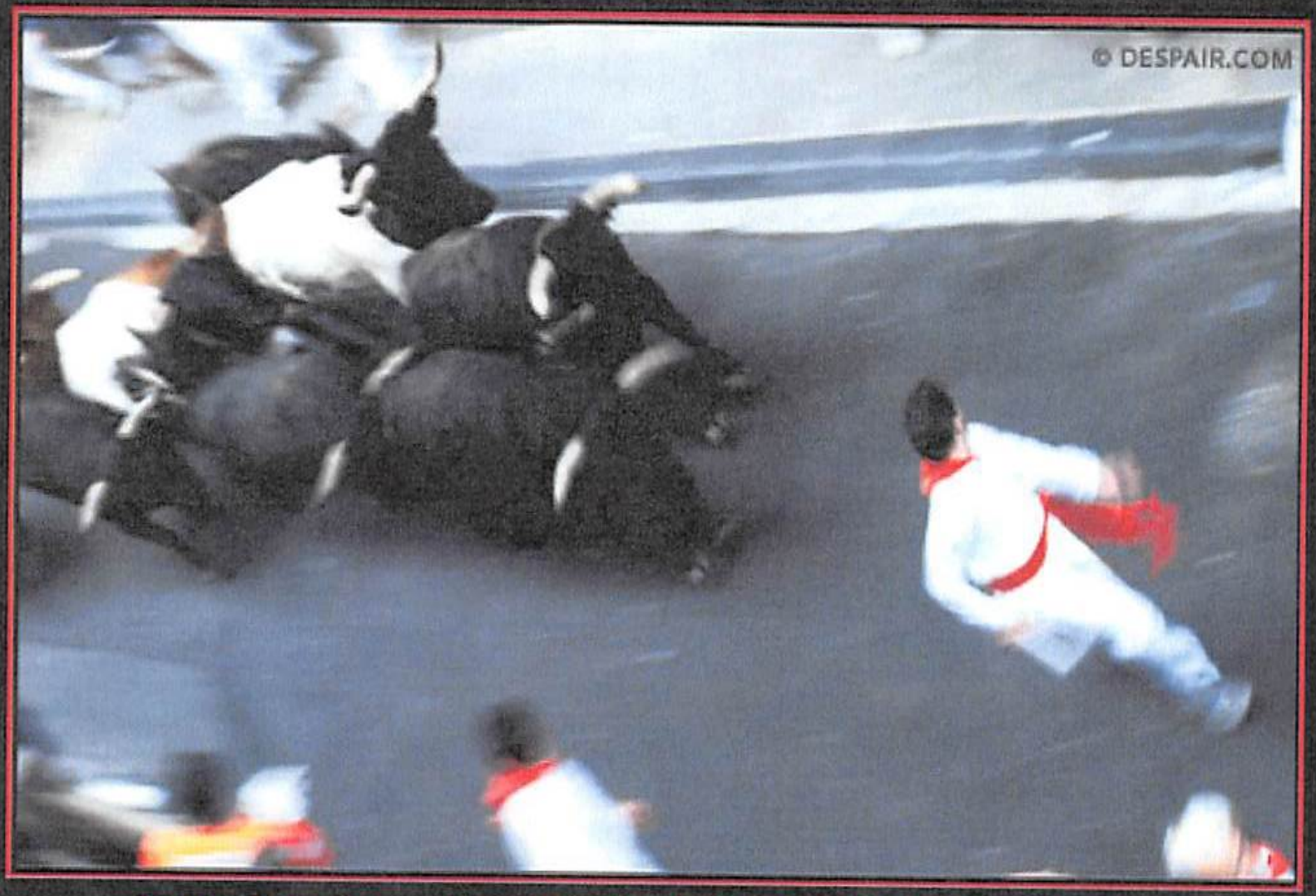
- **FDA Changes:**
  - Generic drug program at FDA
  - Generic drug review in OGD
  - Communication with industry
  - Inspections
- **Industry changes:**
  - Quality of applications
  - Number of review cycles
  - Communication with FDA

GDUFA

- High expectations, especially from industry after fees collected
- Next step is Operations & Implementation
- We are all in this together

GDUFA

- Will not succeed if we just throw additional resources (FTEs, $$) at it AND continue doing the same thing(s)
- Requires:
  - Process identification/mapping
  - Process improvement
  - Strategy to reach goals/metrics
  - Implementation & operationalization



TRADITION

JUST BECAUSE YOU'VE ALWAYS DONE IT THAT WAY
DOESN'T MEAN IT'S NOT INCREDIBLY STUPID.

GDUFA Goals & Commitments

1. GDUFA website

http://www.fda.gov/gdufa

2. GDUFA Commitment Letter

http://www.fda.gov/downloads/ForIndustry/UserFees/GenericDrugUserFees/UCM282505.pdf

YOUR HOMEWORK – READ THE GDUFA COMMITMENT LETTER

GDUFA Review performance goals

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Original ANDA	Expedite review of paragraph IV and maintain pre-GDUFA productivity		60% in 15 months	75% in 15 months	90% in 10 months
Tier 1 first major amendment	Maintain pre-GDUFA productivity		60% in 10 months	75% in 10 months	90% in 10 months
Tier 1 minor amendments (1st – 3rd)	Maintain pre-GDUFA productivity		60% in 3 months*	75% in 3 months*	90% in 3 months*
Tier 1 minor amendments (4th – 5th)	Maintain pre-GDUFA productivity		60% in 6 months*	75% in 6 months*	90% in 6 months*
Tier 2 amendment	Maintain pre-GDUFA productivity		60% in 12 months	75% in 12 months	90% in 12 months
Prior approval supplements	Maintain pre-GDUFA productivity		60% in 6 months*	75% in 6 months*	90% in 6 months*
ANDA, amendment, and PAS in backlog on Oct 1st, 2012	Act on 90% by end of FY 2017				
Controlled correspondences	Maintain pre-GDUFA levels		70% in four months**	70% in two months**	90% in two months**

*10 months if inspection required

** One additional month added to goal if clinical division input required

GDUFA Hiring, procedural, & inspection performance goals

	FY 2013	FY 2014	FY 2015	FY 2016	FY 2017
Hire and train new staff	25% of total	50% of total	25% of total		
Type II DMF completeness assessment – conduct and publish list					
Enhanced refuse to receive standards for ANDAs and related submissions					
Respond to appeals for ANDAs	Within 30 days of receipt				
ANDA teleconference requests	Maintain pre-GDUFA levels		Close-out 200	Close-out 250	Close-out 300
Type II DMF teleconference requests	Maintain pre-GDUFA levels		Limit one per DMF holder per month not to exceed ANDA teleconference levels		
Risk –adjusted biennial CGMP surveillance inspections of generic API and generic finished dosage form manufacturers					Parity of inspection frequency between foreign and domestic firms

GDUFA EFFICIENCY ENHANCEMENTS

ANDA and Type II DMF

- Issue complete response letters reflecting division-levelr eview of deficiencies, including inspections and consults
- Use telephone information requests to address easily correctable deficiencies during the review process
- Issue DMF holder a letter once ANDA referencing DMF is approved or tentatively approved

Regulatory Science

- Convene a working group and consider suggestions from industry and other stakeholders to develop an annual list of regulatory science initiatives for review by CDER Director
- Begin undertaking various regulatory science initiatives upon enactment of the program

Inspections

- Prioritize inspections of establishments associated with ANDAs that are otherwise approvable or eligible for tentative approval except for an outstanding inspection and establishments not inspected previously
- Make inspection classification results and date of the last facility inspection available to the public and industry on FDA's website
- Study foreign government regulator inspections, report findings publicly, and develop a program to utilize foreign inspections classifications when and where appropriate

Systems and Electronic Standards

- Develop API and FDF facility database for self-ID and that links facilities to DMFs and ANDAs
- Develop CMC records database to aid in the efficiency of review and inspection
- Develop and issue electronic data submission standards
- Enhance systems or build databases to implement program requirements

FY2014 USER FEES

Fee Type	GDUFA	PDUFA V
Application	$63,000	$2,169,000 (clinical) $1,084,000 (no clinical)
Supplement	$32,000	$1,084,000 (clinical)
FDF Facility/ Establishment	$220,000-$235,000	$555,000

GDUFA ALSO REQUIRES FACILITIES TO SELF-IDENTIFY

MOVE THE FREIGHT

- **GDUFA Backlog**
  - 2,866 Original ANDAs; 1,868 PAS Supplements
  - New ANDAs
  - > 950
- DMFs for Completeness Assessment
  - ~1,700 ON ~1,400 distinct DMFs
  - Supplements (original)
  - > 5700, ~ 400 are PASs
  - Amendments
  - ~1,900
- Controlled Correspondence
  - ~ 950

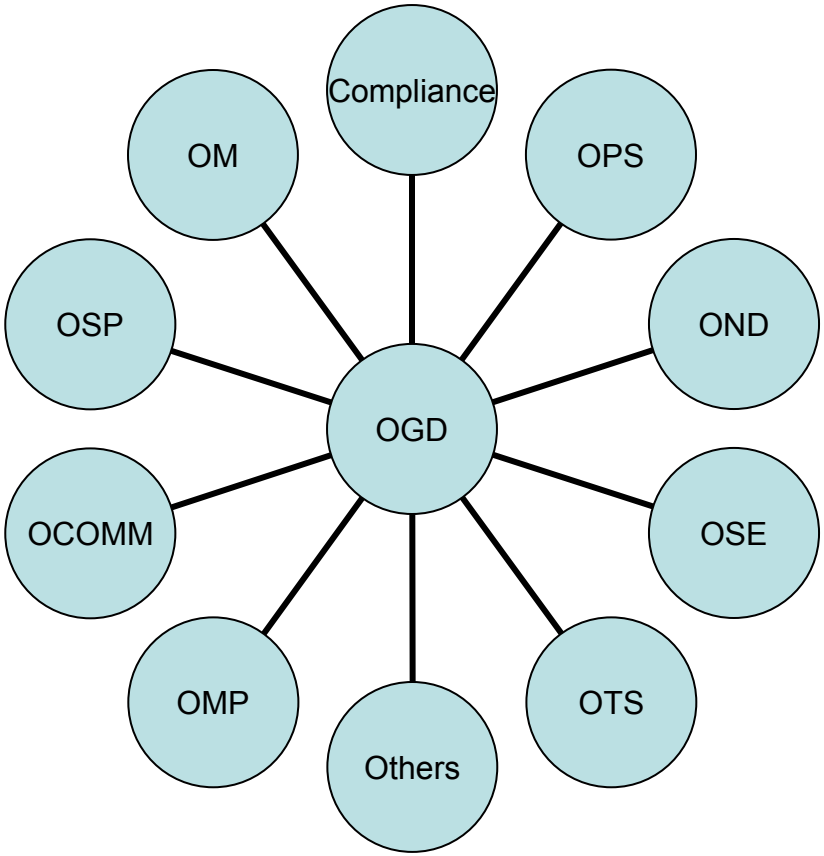
FY2013

Numbers are rounded and do not reflect actual numbers for Congressional reporting purposes

GENERIC DRUG PROGRAM

- Not just OGD
- All of CDER
- Other FDA units:
  - ORA
  - Office of the Commissioner
  - CBER, CDRH

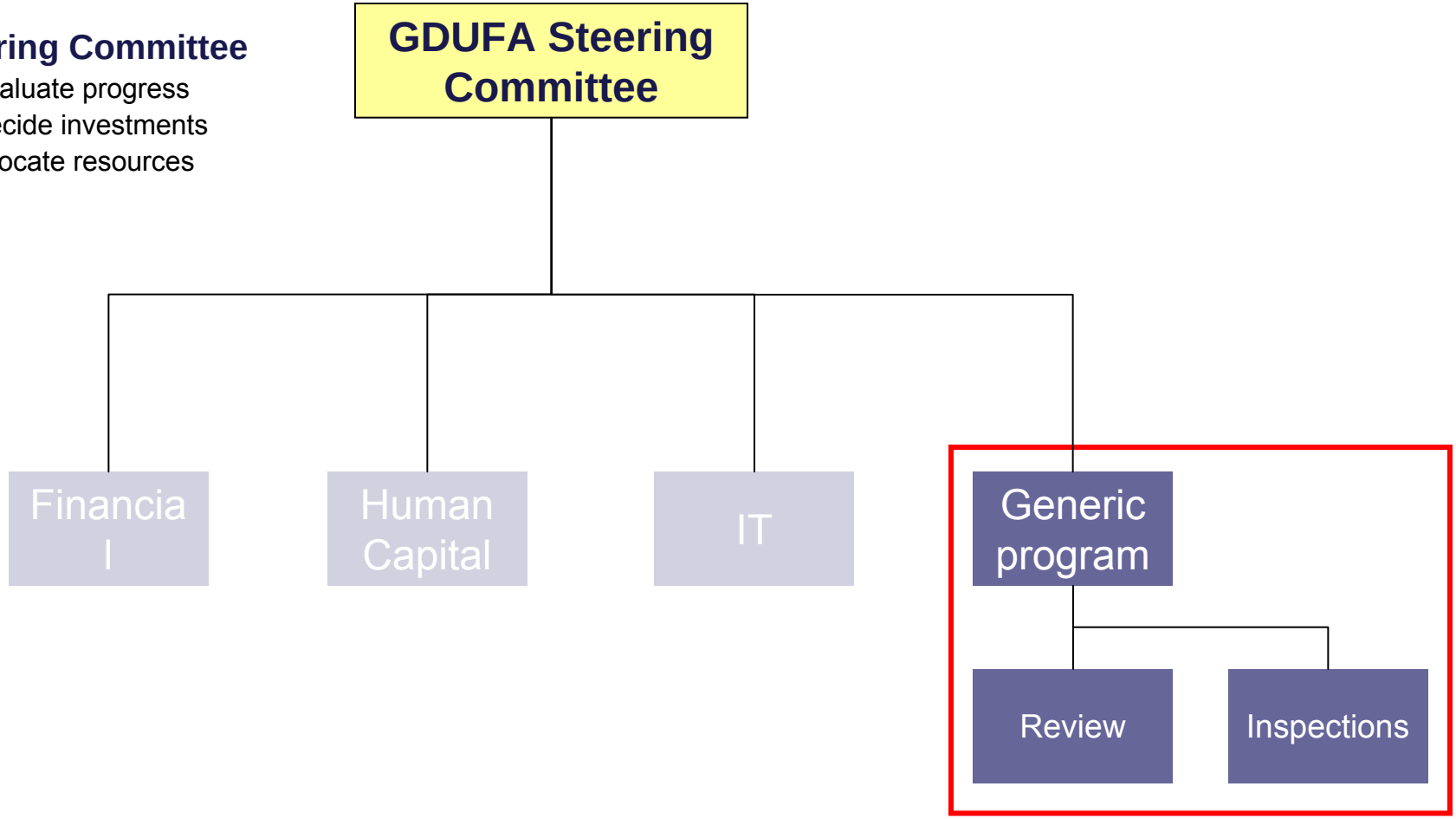
- OGD is the interface for ANDA applicants to interact with the Generic Drug Program



Generic program implementation forms the primary focus going forward

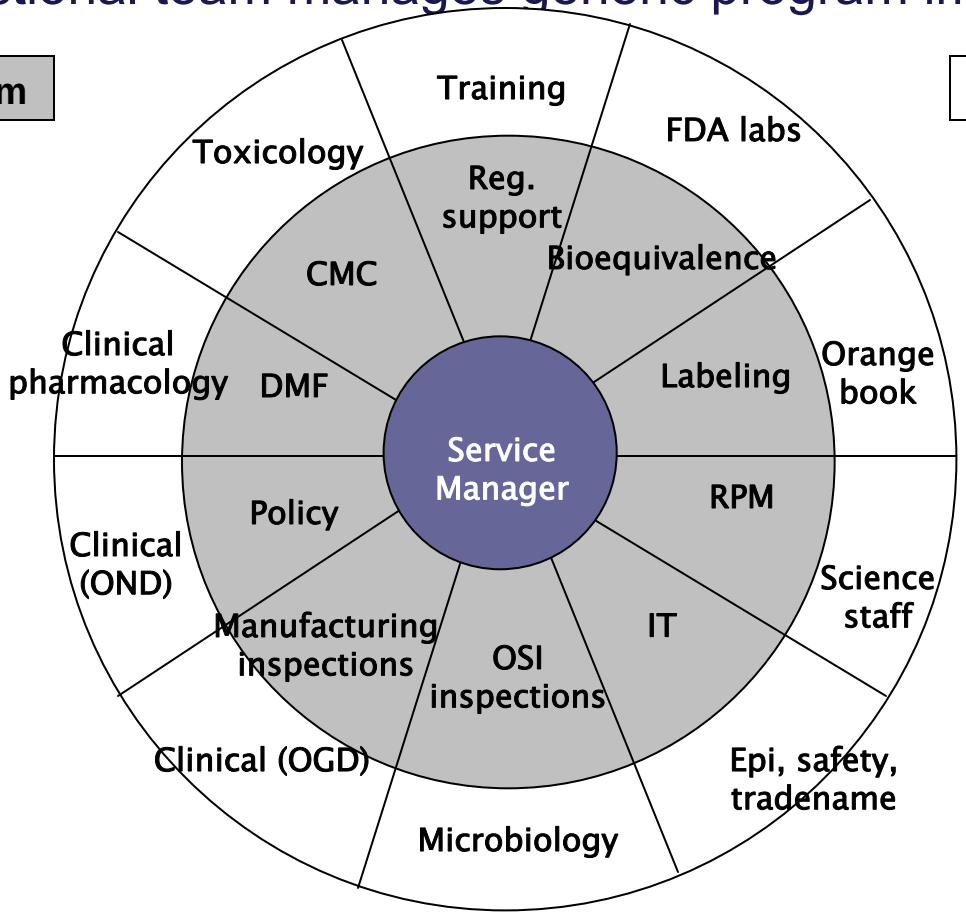
Steering Committee

- Evaluate progress
- Decide investments
- Allocate resources



GDUFA Review Implementation Team (GRIT)

A cross-functional team manages generic program implementation



System that allows identification and tracking

GDUFA Backlog

Original ANDAs

DMFs

Amendments

PASs

Controls

Other work

→ Meet GDUFA goals and metrics

Highlights of GDUFA changes/challenges

1. Complete Response (CR) Letters
2. Easily Correctable Deficiencies (ECDs)
3. Role of RPM
4. Status updates

Complete Response Letters

- "Starting on October 1, 2012 … FDA will issue complete response letters, rather than discipline specific letters, for all ANDAs, including those pending…on October 1, 2012. Complete response letters will reflect division-level review of deficiencies from all relevant review disciplines, including inspections, and ….consults with other agency components..."

GDUFA Commitment letter, page 6.

Complete Response Letters

- FDA/OGD goal to issue CR that is as complete as possible
- No more piece meal deficiencies
- CR will contain Major/Minor deficiencies
- Required internal processes & policy
- Enduring training materials
- Major paradigm shift
  - FDA
  - OGD
  - Industry

Easily Correctable Deficiencies (ECD)

- "FDA reviewers will make every reasonable effort to communicate promptly to applicants easily correctable deficiencies found in the ANDA and will utilize an approach similar to the NDA review process whereby FDA uses telephone information requests to address easily correctable deficiencies during the review process..."

- GDUFA Commitment letter, page 6.

Easily Correctable Deficiencies (ECD)

- Goal is to allow reviewer to complete review
- No definition in Commitment Letter
- If minor/major deficiency, it is **NOT** an ECD
- Need to revise internal processes on ECDs
  - Guidance Major/Minor/Telephone Amendments, 2001
  - MaPP 5240.7, 2003
  - Internal CR IQP/SOP, 2010(?)
- Need to train OGD & have enduring training materials

Communications

- Role of Regulatory Project Manager (RPM)
- Previous Project Mgmt in OGD was siloed
- No one responsible for application from door to door
- No central point of contact
- Imperative need to meet goals

Regulatory Project Manager (RPM)

- **"THE"** Point of Contact is the Regulatory Project Manager
  - Centralize Communication Flow vs. past Siloed practices
  - Good communication practices
  - Consistency
  - Streamlines
  - Documentation of communication
- Allows reviewers to **REVIEW**
- Consistent with FDA practices with other product Centers and other User Fee Programs

Status Updates

- FDA recognizes the importance of these and industry desire to launch on Day 1
- We value constructive input and collaboration
- PAST: Reactive, crisis management mode
  - Fishing expedition, shopping around
  - OGD "sold out" other Agency colleagues
- NOW: Proactive, systematic **process** that meets goal dates – we are working on it

INDUSTRY CHANGES

INDUSTRY CHANGES

- GDUFA is a commitment between FDA and Industry
- Requires changes to both parties
- What is industry doing because of GDUFA?
- How will that get us to meeting goals?

Request: Industry Changes

- One point of contact for the RPMs
- Consistent with FDA practices with other product Centers and other User Fee Programs

Industry (cont)

Shore up Business Partners:

- Arrears list
  - Know who is on it
- Confidentiality agreements
  - (e.g., Letter of Authorization) with API suppliers and sites (your contractors)
  - FDA cannot discuss with ANDA holder without divulging CCI or TS information found in DMF

Industry (cont)

Submissions:

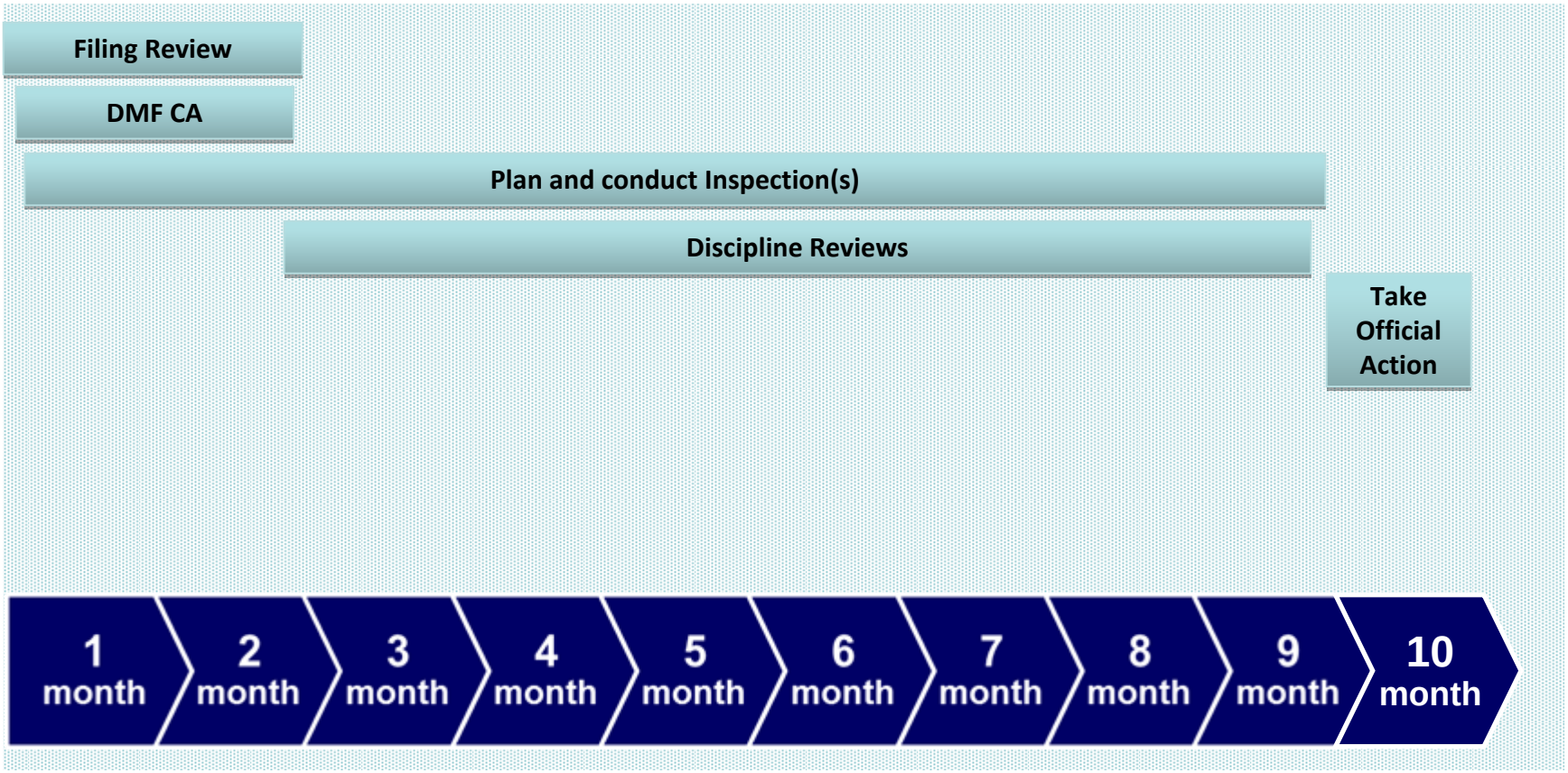
- Electronic submissions
  - GDUFA applies ONLY to eSubs
  - Submit in eCTD format
- Ensure that 356h submission is accurate, complete, and identifies all sites

Industry (cont)

DMF Completeness Assessment (CA)

- DMFs should be submitted well in advance of ANDA in order for CA to be conducted
- Submit ~6 months in advance
- Allows time for industry to respond to DMF incomplete letter
- GDUFA Years 1 & 2 – industry has gotten a free pass being able to submit DMF with ANDA.
- GDUFA Year 3 and beyond – may be grounds for RTR

Simplified ANDA review process



Industry (cont)

Complete Response (CR) letters

- Adequate response addresses ALL deficiencies received in the CR
- Partial response will not be accepted
  - Will not be processed as a resubmission
  - Will not start a new review cycle
- Timely response
  - Within 1 year
  - Can enforce 21 CFR 314.65
  - Administratively withdraw application
  - O/w abusing the system and wasting GDUFA resources

Industry (cont)

Complete Response (CR) letters

- "Within one year after the date of this letter, you are required to resubmit or take other actions available under 21 CFR 314.110. If you do not take one of these actions, we may consider your lack of response a request to withdraw the application under 21 CFR 314.65..."
- FDASIA requirement to report number of days applications are **pending** with industry & with FDA

Industry (cont)

- **Easily correctable deficiency (ECDs)**
  - Timely response
  - Within 10 US business days
  - Allows OGD reviewers to finish their reviews
  - Moves us toward being able to issue action
    - CR, TA or approval
  - Still may get major/minor deficiencies in CR

Industry (cont)

- Industry Motto: File First, Develop Later
  - Poorly assembled applications
  - Poor quality applications
  - Leading to multiple-cycle reviews
- Inefficient use of GDUFA resources
- Improve quality of submissions
- Decrease number of review cycles

ANDA AMENDMENTS

	Solicited Amendments Goals	Unsolicited Amendments Goals
TIER 1	1st Major: 10 months 1st – 3rd Minor: 3 months 4th & 5th Minor: 6 months	Delaying action*or otherwise would eventually be solicited: 3 months
TIER 1	Any TIER 1 amendment requiring an inspection: 10 months	
TIER 2	N/A	Amendment not arising from "delaying action": 12 months
TIER 3	≥ 2nd Major: No goal ≥ 6th Minor: No goal	N/A

*Indicated by sponsor and agreed by FDA

GDUFA Accomplishments

Industry Accomplishments

- Fees paid
  - FDA collected close to goal of $299 million
- Self identification
  - ~2,200 sites
  - Foreign > domestics sites
  - API > FDF

FDA Accomplishments

- FDA HIT ALL YEAR 1 DELIVERABLES
- **FDA HIT ALL YEAR 1 DELIVERABLES**
- **FDA HIT ALL YEAR 1 DELIVERABLES**

GDUFA Hiring & Training

- Goal: hire 25%
- FDA met and exceeded GDUFA Year 1 hiring goals

GDUFA BACKLOG

- 2866 original ANDAs
- 1882 PAS supplements

First Actions in FY2013 (reportable metric):

- >1,600 actions issued (~35%)
  - CR with inspection (#1)
  - Approval or TA (#2)
  - RTR
  - Withdrawal

Numbers are rounded and do not reflect actual numbers for Congressional reporting purposes

GDUFA COMMUNICATIONS

- Complete Response Letters for ANDAs
- Total CRs Issued ~1,250
  - Majority were for GDUFA backlog 1st action
  - FY2012 issued less than 50 CRs

  - ~560 with inspections
  - ~690 **WITHOUT inspections**
    - Are not part of GDUFA metrics/commitments
    - Communicating with industry
    - Transparency

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GDUFA COMMUNICATIONS

GDUFA DRAFT GUIDANCES:

- GDUFA Questions & Answers x 2
- DMF Completeness Assessment
- Refuse to Receive
- Fee Types

- FDA issued ALL guidances required under GDUFA

GDUFA COMMUNICATIONS

- FDA GDUFA website –www.fda.gov/gdufa
  - Info about stakeholder meetings (public, small business), technical walk-throughs, webinars, multiple language Fact Sheets
- Helpdesk on GDUFA
  - AskGDUFA@fda.hhs.gov, (866) 405-5367
  - Answered >1,000 questions since May 2012
- GDUFA listserve
- DMF "available for reference" list, since December 2012
- GPhA, AAPS, DIA & other professional/scientific groups

GDUFA COMMUNICATIONS

- FDA - GPhA Board of Directors Quarterly meetings
  http://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/approvalapplications/abbreviatednewdrugapplicationandagenerics/ucm370616.htm

GDUFA ACCOMPLISHMENTS

GDUFA FY2013 Regulatory Science

- Only user fee program with Regulatory Science!
- New External & Internal Collaborations
  - 20 Grants, 8 Contracts
  - Lab equipment
  - ORISE fellows
- ~ $20 million
- May 2013, Part 15 for public input on FY2014 GDUFA regulatory science priorities – posted before end of FY2013

http://www.fda.gov/Drugs/NewsEvents/ucm367997.htm
http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/ucm370952.htm

FY2013 Approvals

- ANDA Approvals
  - > 425
  - (FY2012, ~500)
- PASs approvals
  - >560
  - (FY2012, ~260)
- TAs
  - > 90
  - (FY2012, ~100)

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Non-GDUFA GUIDANCES

- NEW BE guidances - ~60
  - Key Products:
    - Albuterol sulfate
    - Buproprion Hydrochloride
    - Ferumoxytol
    - Fluticasone propionate/salmeterol xinafoate
    - Sodium ferric gluconate
- Revised BE guidances - ~40
- Stability Guidance & accompanying Q&A

OGD UPDATES

OGD Priorities

1. GDUFA

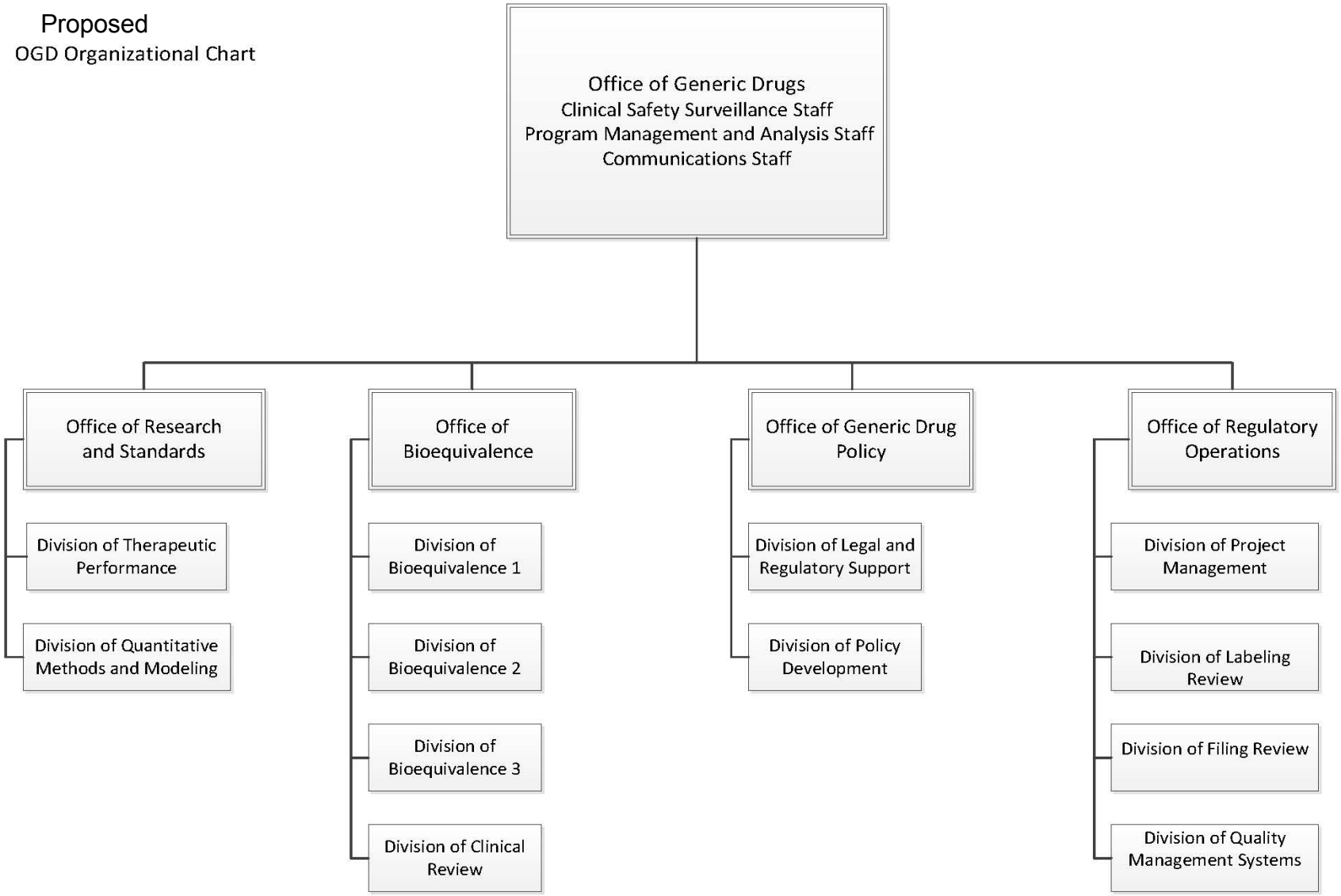
2. GDUFA

3. **GDUFA**

Major Reorganizations

- OPQ reorg
  - All CDER product quality reviews
  - OGD chemistry and microbiology review functions
- OGD reorg to a Super Office

Proposed
OGD Organizational Chart



OGD CHALLENGES

- GDUFA implementation
- Hiring under GDUFA
- Training new hires
- Identifying key leadership
- Budget changes
- Office space

- Move to White Oak in 2014

OGD GDUFA Year 1 hires

- >100 new hires to OGD in FY2013
- MAJOR FOCUS – CMC REVIEWERS
  - experience in formulation, process, and manufacturing science
  - ~65 FTEs

OGD GDUFA

Virtual Hiring Event – November 4

- Chemical Engineer
- Chemist
- Microbiologist

} **OPQ**

- Regulatory Project Manager
- Consumer Safety Officer
- Regulatory Support Specialist

- Regulatory Counsel
- Public Health Analyst
- Health Science Analyst
- Writer-editor

- Pharmacist
- Pharmacologist
- Pharmacometrics
- Interdisciplinary Scientist
- Medical Officer
- Toxicologist

- Health Communication Specialist

- Quality Management Specialist
- Staff Development Specialist

- Administrative personnel

http://www.fda.gov/AboutFDA/WorkingatFDA/GenericDrugUserFeeHiring/default.htm

Why do we have to get it right with GDUFA?











IMPLEMENTING GDUFA is a shared responsibility

Urgency
Ownership
Accountability
Commitment

THANK YOU!