Office of Generic Drugs (OGD)
Update on GDUFA Implementation

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Director, Office of Generic Drug
CDER/FDA

GPhA CMC Workshop
May 17, 2016
OUTLINE

1. Opening Comments
2. GDUFA Update
3. Output & Productivity
4. ANDA “approvability”
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GENERIC DRUG PROGRAM

- Not just OGD
- All of CDER
- Other FDA units:
  - ORA
  - Office of the Commissioner
  - OCC
  - CDRH, CBER
- OGD is the interface for ANDA applicants to interact with the Generic Drug Program
GDUFA IMPLEMENTATION

- Agency is meeting **ALL** of its obligations under the GDUFA commitment letter
- We are going above and beyond the commitments
- Building a modern, 21st Century generic drug program
- Resulting in significant and sustained increase in communications, actions & approvals
OUTLINE

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GDUFA

MAJOR PROGRAM GOALS

(5 year plan)

1. Metrics
   - Applications
   - GDUFA Backlog
   - cGMP Inspections

2. Efficiency enhancements

3. Regulatory science

http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/default.htm
# GDUFA GOAL DATES

Powerful tool to improve the timeliness and predictability of review

<table>
<thead>
<tr>
<th>Goals</th>
<th>Review Time</th>
<th>FY2015</th>
<th>FY2016</th>
<th>FY2017</th>
</tr>
</thead>
<tbody>
<tr>
<td>Original ANDA submission</td>
<td>15 months</td>
<td>60%</td>
<td>75%</td>
<td>90%~</td>
</tr>
<tr>
<td>Tier 1 first major amendment</td>
<td>10 months</td>
<td>60%</td>
<td>75%</td>
<td>90%</td>
</tr>
<tr>
<td>Tier 1 minor amendments (1st-3rd)</td>
<td>3 months*</td>
<td>60%</td>
<td>75%</td>
<td>90%</td>
</tr>
<tr>
<td>Tier 1 minor amendments (4th-5th)</td>
<td>6 months*</td>
<td>60%</td>
<td>75%</td>
<td>90%</td>
</tr>
<tr>
<td>Tier 2 amendment</td>
<td>12 months</td>
<td>60%</td>
<td>75%</td>
<td>90%</td>
</tr>
<tr>
<td>Prior Approval Supplements</td>
<td>6 months*</td>
<td>60%</td>
<td>75%</td>
<td>90%</td>
</tr>
<tr>
<td>ANDA teleconference requests</td>
<td>10 business days</td>
<td>200</td>
<td>250</td>
<td>300</td>
</tr>
<tr>
<td>Controlled correspondence*</td>
<td>2 months</td>
<td>70%^</td>
<td>70%</td>
<td>90%</td>
</tr>
</tbody>
</table>

ANDAs, amendments and PASs in backlog on Oct 1, 2012

Act on 90% by end of FY2017

Note: Performance goals in the chart means FDA should take a “first action” (as defined above) on a certain percent of applications, etc. within the timeframes listed; it does not mean FDA should approve applications, etc. within such timeframes.

*If no input required from clinical division

*10 months if inspection required

^4 months

~10 months

http://www.fda.gov/ForIndustry/UserFees/GenericDrugUserFees/default.htm
GDUFA IMPLEMENTATION

*Build the Machine*

- Deep foundational restructuring
- Build infrastructure
- Improve business processes
- Hire and train new staff
- New IT platform
- Improve communications

- All to prepare for Year 3 Goal Dates **AND** to enable us to hit goal dates
OGD & OPQ believe, in working with Industry, by Year 5 the 1st cycle approvability rate for ANDAs can be improved. This goal is achievable provided that upon first submission, the ANDAs are of high quality and complete to allow for FILING & Scientific Review, i.e. ANDA “approvability.”
GDUFA

TRANSFORM THE PROGRAM
and
PERFORM WHILE TRANSFORM

We built the machine…
NOW we are cranking it up!
OUTLINE

1. Opening Comments
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INCOMING FROM INDUSTRY
PROJECTED vs ACTUAL ANDA RECEIPTS

FDA Received
Approximately
5.5 Years of Projected
ANDA Receipts in 4 years

750 Projected
ANDAs per year

*Numbers are based on current data and will be further scrubbed for formal reporting purposes.
Monthly ANDA Receipts

*Numbers are based on current data and will be further scrubbed for formal reporting purposes*

**CONTROLLED CORRESPONDENCE RECEIPTS**

### Controlled Correspondences Received under GDUFA (by discipline) FY13 - FY15

<table>
<thead>
<tr>
<th>Office of Bioequivalence (Division of Bioequivalence)</th>
<th>Office of Bioequivalence (Division of Clinical)</th>
<th>Office of Generic Drug Policy (Orange Book &amp; Policy)</th>
<th>Office of Pharmaceutical Quality (Chemistry)</th>
<th>Office of Regulatory Operations (Division of Filing &amp; Division of Labeling Review &amp; Immediate Office)</th>
<th>Office of Research &amp; Standards</th>
<th>Grand Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>141</td>
<td>35</td>
<td>9</td>
<td>78</td>
<td>552</td>
<td>138</td>
<td>1519</td>
</tr>
<tr>
<td>225</td>
<td>29</td>
<td>29</td>
<td>184</td>
<td>502</td>
<td>118</td>
<td>1087</td>
</tr>
<tr>
<td>322</td>
<td></td>
<td>91</td>
<td>269</td>
<td>555</td>
<td>257</td>
<td>953</td>
</tr>
</tbody>
</table>

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OUTPUT from FDA

- GDUFA Backlog
- ANDAs
- PASs
- Filing
- Communication
- Controlled Correspondence
- Guidance
Total ANDA Regulatory Actions per Month
(AP+TA+CR+RTR)
## OVERALL ACTIONS

<table>
<thead>
<tr>
<th></th>
<th>PRE-GDUFA</th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FY2012</td>
<td>FY2013</td>
<td>FY2014</td>
<td>FY2015</td>
</tr>
<tr>
<td>ANDA approvals</td>
<td>517</td>
<td>440</td>
<td>409</td>
<td>492</td>
</tr>
<tr>
<td>Tentative Approval (TA)</td>
<td>102</td>
<td>95</td>
<td>91</td>
<td>120</td>
</tr>
<tr>
<td>PAS approvals</td>
<td>275</td>
<td>535</td>
<td>659</td>
<td>624</td>
</tr>
<tr>
<td>Complete Response (CR)</td>
<td>84</td>
<td>1251</td>
<td>1254</td>
<td>1180</td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>978</td>
<td>2321</td>
<td>2413</td>
<td>2416</td>
</tr>
<tr>
<td>DMF Completeness Assessment (CA)</td>
<td>0</td>
<td>1699</td>
<td>1706</td>
<td>901</td>
</tr>
</tbody>
</table>

**FDA will aspire to the extent possible to maintain levels of productivity at least similar to pre-GDUFA levels, while hiring and training incremental staff necessary to achieve the program performance goals, building necessary systems and implementing outlined program changes in years 1 and 2 of the program (GDUFA Commitment Letter, page 3) [http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm375079.htm](http://www.fda.gov/Drugs/DevelopmentApprovalProcess/HowDrugsareDevelopedandApproved/ApprovalApplications/AbbreviatedNewDrugApplicationANDAGenerics/ucm375079.htm)**
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Prior Approval Supplements (PAS) Exceeding GDUFA Review Goals*

*Goal dates provided through April 2015, as those are the goal dates that have actually accrued. The cohort data is not mature enough to report on whole year data.

Numbers are based on current data and will be further scrubbed for formal reporting purposes.

# GDUFA Backlog Applications with First Action through 3/31/2016

<table>
<thead>
<tr>
<th>Actions</th>
<th>ANDAs</th>
<th>PASs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number with First Action*</td>
<td>2,516</td>
<td>1,691</td>
</tr>
<tr>
<td><strong>Percentage Complete</strong></td>
<td>88%</td>
<td>90%</td>
</tr>
<tr>
<td>Approval</td>
<td>632</td>
<td>970</td>
</tr>
<tr>
<td>Tentative Approval</td>
<td>158</td>
<td>4</td>
</tr>
<tr>
<td>Complete Response with an Inspection**</td>
<td>1441</td>
<td>470</td>
</tr>
<tr>
<td>Refuse to Receive</td>
<td>69</td>
<td>2</td>
</tr>
<tr>
<td>Withdrawn Application</td>
<td>216</td>
<td>245</td>
</tr>
</tbody>
</table>

* Numbers reflect data available at the time of report publication and may change based on refreshed counts in our tracking systems, including application status updates. These numbers are not intended for Congressional reporting purposes.

**Complete Response with an Inspection is a written FDA communication to an applicant usually describing all of the deficiencies that the agency has identified in an application that must be satisfactorily addressed before it can be approved.

**GDUFA BACKLOG:**
2,866 original ANDAs
1,873 PAS supplements

**GDUFA GOAL:**
90% get first ACTION by end of GDUFA YR 5 (9/30/2017)
PRODUCTIVITY:
COMMUNICATION WITH INDUSTRY
EASILY CORRECTABLE DEFICIENCIES (ECDs) & INFORMATION REQUESTS (IRs)

OVER 4,700 communications to industry last FY during ANDA review

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Exceeding Controlled Correspondence Goals

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Application “approvability”

Upon first submission, the ANDAs are of high quality and complete to allow for:

(1) Filing
(2) Scientific Reviews
How “approvable” is your ANDA?
Is it complete?

For Filing

- NO
  - RTR

- YES
  - Received

For Scientific Review

- NO
  - Multiple Review Cycles

- YES
  - 1st cycle approval
## Cohort Year 3 APPROVALS

*Through 3/31/16 (15 month goal)*

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>ANDA Number</th>
<th>Company</th>
<th>Date of Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tretinoin</td>
<td>207955</td>
<td>Spear</td>
<td>08/13/2015</td>
</tr>
<tr>
<td>Loperamide*</td>
<td>206548</td>
<td>Aurobindo</td>
<td>12/15/2015</td>
</tr>
<tr>
<td>Gabapentin</td>
<td>206402</td>
<td>Alkem</td>
<td>12/23/2015</td>
</tr>
<tr>
<td>Sodium Polystyrene**</td>
<td>206815</td>
<td>Invatech</td>
<td>2/18/2016</td>
</tr>
<tr>
<td>Desoximetasone</td>
<td>208101</td>
<td>Teligent</td>
<td>2/25/2016</td>
</tr>
<tr>
<td>Fluticasone</td>
<td>208150</td>
<td>Apotex</td>
<td>2/29/2016</td>
</tr>
<tr>
<td>Levonorgestrel</td>
<td>207976</td>
<td>Novast</td>
<td>3/11/2016</td>
</tr>
<tr>
<td>Desipramine</td>
<td>208105</td>
<td>Amneal</td>
<td>3/17/2016</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>208077</td>
<td>Amneal</td>
<td>3/18/2016</td>
</tr>
</tbody>
</table>

AP issued on or before GDUFA goal date
*Not a first cycle AP
** AP issued after GDUFA goal date

Information available at: Drugs@FDA website: http://www.accessdata.fda.gov/scripts/cder/drugsatfda/index.cfm
# Cohort Year 3 TENTATIVE APPROVALS (TA)

*Through 3/31/16 (15 month goal)*

<table>
<thead>
<tr>
<th>Active Ingredient</th>
<th>ANDA Number</th>
<th>Company</th>
<th>Date of Tentative Approval</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diclofenac</td>
<td>208068</td>
<td>Paddock</td>
<td>10/14/2015</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>208098</td>
<td>Taro</td>
<td>01/14/2016</td>
</tr>
<tr>
<td>Sildenafil*</td>
<td>206401</td>
<td>Ajanta</td>
<td>01/21/2016</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>208031</td>
<td>Lupin</td>
<td>01/25/2016</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>208037</td>
<td>MSN Labs</td>
<td>01/25/2016</td>
</tr>
<tr>
<td>Lurasidone</td>
<td>208066</td>
<td>Sun Pharma</td>
<td>01/25/2016</td>
</tr>
<tr>
<td>Risedronate</td>
<td>205280</td>
<td>Orchid</td>
<td>01/29/2016</td>
</tr>
<tr>
<td>Lurasidone*</td>
<td>208055</td>
<td>Torrent</td>
<td>02/5/2016</td>
</tr>
<tr>
<td>Lurasidone*</td>
<td>208058</td>
<td>Emcure</td>
<td>02/23/16</td>
</tr>
<tr>
<td>Aspirin + dipyridamole ER</td>
<td>207944</td>
<td>Par</td>
<td>03/1/2016</td>
</tr>
<tr>
<td>Clofarabine</td>
<td>208167</td>
<td>Zydus</td>
<td>03/4/2016</td>
</tr>
<tr>
<td>Efavirenz, Emtricitabine, tenofovir</td>
<td>206894</td>
<td>Cipla</td>
<td>03/22/2016</td>
</tr>
</tbody>
</table>

TA issued on or before GDUFA goal date

*Not a first cycle TA*
ANDA “Approvability”
(Cohort Year 3: submitted October-December 2014 with GDUFA Goals (15 month) in January-March 2016, n=119)

- >95% met GDUFA goals
- 14% application first cycle approval/TA
  - Bioequivalence – 72% approvable
- 63% complete response
  - CR leads to subsequent or multiple review cycles
  - Majority related to CMC unresolved deficiencies and inadequate facilities
  - Despite numerous OPQ IR’s during 15 month review cycle

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ANDA “Approvability”
(Cohort Year 3: January to March 2016, n=119)

• >95% met GDUFA goals
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In Years 3 & 4 --- 15 month GDUFA goals
In Year 5 --- 10 month GDUFA goals
Number of information requests (IR’s) decreases with shorter goals
CONCLUSIONS
YEAR 3 METRIC GOALS
How are we doing?

• FDA met or exceeded all Year 3 metric goals
• See GDUFA performance reports

http://www.fda.gov/AboutFDA/ReportsManualsForms/Reports/UserFeeReports/PerformanceReports/ucm384247.htm
YEAR 4 METRIC GOALS
How are we doing?

- GDUFA Backlog – will hit 90% metric soon
- PASs & Controls – exceeding goals
- Original ANDAs and amendments – too soon to tell and looking good

- Application “Approvability” – too soon to tell (not a GDUFA metric)
WHAT IS NEXT?

Years 5:

• Review metrics tighten - original ANDAs 90% in 10 months

• Up months and down months

Strong focus on:

• Meeting TADs and related communications

• First generics: Avoid FTF PIV forfeitures, pursue timely first generic approvals
FDA Delivering on GDUFA

- FDA is fulfilling its GDUFA commitments
- In many cases, we are going above and beyond our negotiated commitments
- We are building a robust, modern generic drug regulatory program
  - Sustainable and predictable
  - Clear and consistent communication
  - Fairness across applications and applicants
This CMC Workshop….

• Hoping that information provided to industry translates into less CMC deficiencies or rapidly correctable ones
• Need industry’s assistance in implementing lessons learned to produce first cycle approvals and decreased review cycles
THANK YOU!