



GD(UFA)

U.S. Food and Drug Administration

Generic Drug User Fee Amendments of 2012

<http://www.fda.gov/gdufa>

Draft Guidance for Industry: *ANDA Submissions – Amendments and Easily Correctable Deficiencies Under GDUFA*

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GDUFA Goal Information

- Beginning on October 1, 2014 (FY 2015 or Cohort Year 3 of the GDUFA program), GDUFA goals will apply to electronically-submitted amendments to original ANDAs, and amendments to prior approval supplements (PAS)
- ANDA is assigned a cohort year based on the FY in which the original ANDA was first submitted
 - Once an ANDA is assigned to a certain cohort year, the submission of subsequent amendments will not change that ANDA's cohort year
- GDUFA Performance Goals only apply to an amendment if the original ANDA or PAS being amended was submitted in Cohort Year 3 or after
 - Example: An original ANDA is submitted on September 30, 2014 (Cohort year 2). An amendment is submitted on September 30 (2016) Cohort Year 4. No GDUFA performance goal date will be assigned to that amendment

Amendment Performance Goal Basics

- All amendment performance goals are incremental and are calculated from the date of the amendment electronic submission
 - **PRE-FDA** action (PRE-CR) *adjusts* the performance goal date and is additive
 - **POST-FDA** action (POST-CR) sets a *new* performance goal date
- Amendment performance goals never shorten the ANDA goal date
- Amendments containing multiple elements – longest performance goal date applies

GDUFA Amendment Terminology

- **Solicited:**
 - Submitted at the request of FDA in response to a CR letter
- **Unsolicited:**
 - Submitted on the applicant's own initiative
- **Delaying:**
 - Submitted on the applicant's own initiative to address actions by a third party that would cause delay or impede application review or approval timing and that were not a factor at the time of submission
- **Tiers:**
 - Determine how performance goals apply to amendments
- **Administrative:**
 - Amendment that is routine in nature and does not require scientific review

GDUFA Amendment Tiers

- Tier 1
- Tier 2
- Tier 3
- Administrative

GDUFA Amendment Tiers: Tier 1

- All **solicited** 1st MAJOR and the 1st five MINOR amendments
- All **unsolicited** amendments indicated by sponsor and agreed by FDA to be a result of a delaying action or otherwise would eventually be solicited (*aka delaying amendment*)
- **Tier 1 Goal Dates:**
 - 1st MAJOR amendment = 10-month goal
 - 1st – 3rd MINOR amendments = 3-month goal
 - 4th & 5th MINOR amendments = 6-month goal
 - Any Tier 1 amendment requiring an inspection = 10-month goal

GDUFA Amendment Tiers: Tier 2

- Any **Unsolicited** Change
 - Gratuitous amendments not arising from “delaying action”
 - Changes made not by the RLD or at FDA’s request
 - Example: new facilities
- **Tier 2 Goal Dates:**
 - All Tier 2 = 12-month goal

GDUFA Amendment Tiers: Tier 3

- All **solicited** MAJOR amendments subsequent to the 1st MAJOR amendment
- All **solicited** MINOR amendments subsequent to the 5th MINOR amendment
- **Tier 3 Goal Dates:**
 - $\geq 2^{\text{nd}}$ MAJOR amendment = no GDUFA performance goal
 - $\geq 6^{\text{th}}$ MINOR amendment = no GDUFA performance goal

GDUFA Amendment Tiers: Administrative

- Neither Tier 1, Tier 2 nor Tier 3
- Will not impact the original review goal date
- Routine and administrative in nature
- Do not require scientific review
- Examples: General correspondence, patent amendments, requests for final approval (with no scientific changes to ANDA)

Summary: Amendment Performance Goals

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

*10 months if an inspection is required

Guidance Purpose & Goals

- Purpose:
 - Assist applicants preparing to electronically submit amendments to ANDAs or PASs by explaining how GDUFA performance goals apply to amendments
- Goals:
 - Incentivize submissions of high-quality original applications
 - Decrease the number of review cycles by demonstrating the penalty of extending or eliminating the review clock

Guidance Overview

- Describes:
 - Classification of major amendments, minor amendments, and ECDs
 - Amendment tiers
 - GDUFA amendment performance goal dates
 - Submission process
 - Requests for reconsideration

Guidance Overview: Amendments

- Solicited
 - Major
 - Minor
 - ECD
- Unsolicited
 - Delaying
 - Non-delaying
- Administrative

Changes to 2001 Guidance

Guidance for Industry

Major, Minor, and Telephone Amendments to Abbreviated New Drug Applications

Comments and suggestions regarding this document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the guidance. Submit comments to Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document contact Rita Hassall (301)827-5845

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
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Revision 2
OGD

Changes re: Major Amendments

Then (2001)

Major amendments have the same review priority as original, unreviewed ANDAs and are reviewed in accordance with OGD's first in-first reviewed procedure

Now (2014)

FDA review of a major amendment requires a ***substantial expenditure*** of FDA resources.

Major amendments contain a substantial amount of new data or new information not previously submitted to or reviewed by FDA.

Changes re: Minor Amendments

Then (2001)

Minor amendments have a higher priority than major amendments because they often mean an application is close to approval and should, therefore, be given priority. Except for those amendments that are classified as major or telephone, amendments will be designated as minor. Minor amendments often consist of deficiencies that are outside the control of the applicant or deficiencies that are more easily addressed than those in a major amendment.

Now (2014)

FDA review of a minor amendment requires **fewer FDA resources than are necessary to review a major amendment** but more than are necessary to review the information submitted in response to an easily correctible deficiency.

Changes re: Telephone Amendments

Then (2001)

If an amendment would otherwise be classified as minor, but the deficiencies are of a limited number or complexity, it can be classified as a telephone amendment at the discretion of the reviewer's team leader. The applicant should provide a complete and satisfactory response within 10 calendar days of the call.

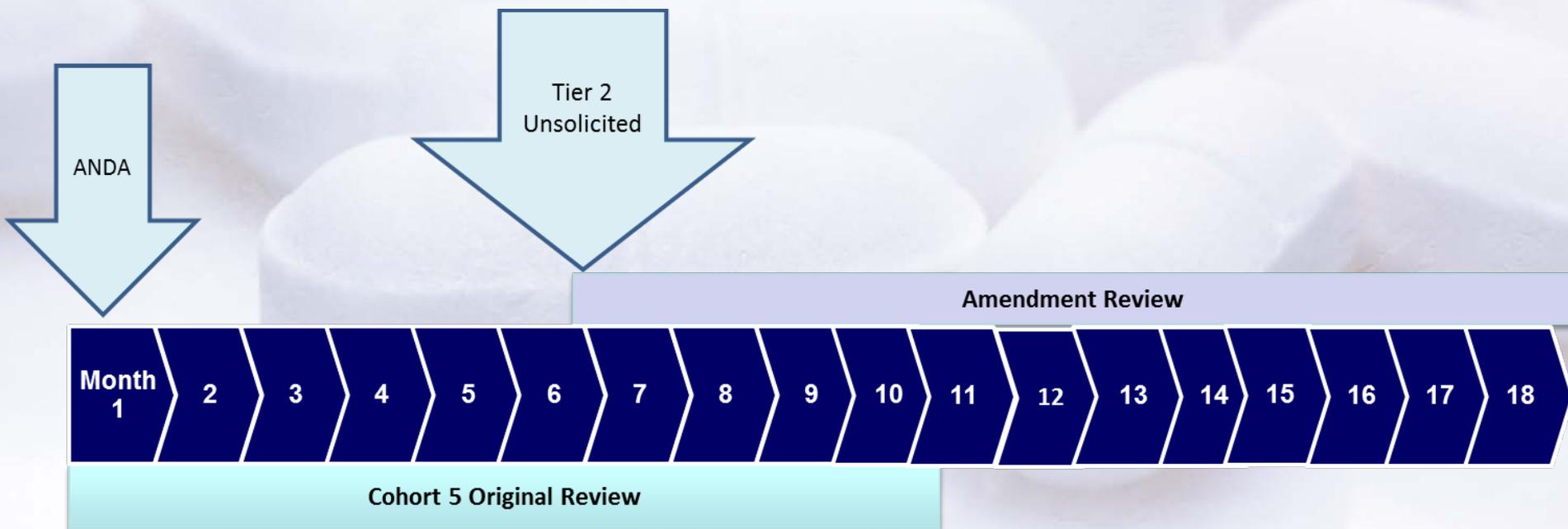
Now (2014)

FDA review of information submitted in response to an easily correctible deficiency (ECD) will require **only a modest expenditure of FDA resources**.

An applicant should be able to respond to an ECD quickly as the applicant should already possess or be able to quickly retrieve the information needed for an adequate response to an ECD.

Example: Pre-CR Amendments

An unsolicited amendment with a 12-month performance goal date submitted 4 months prior to the original goal date adds 8 months to the review clock



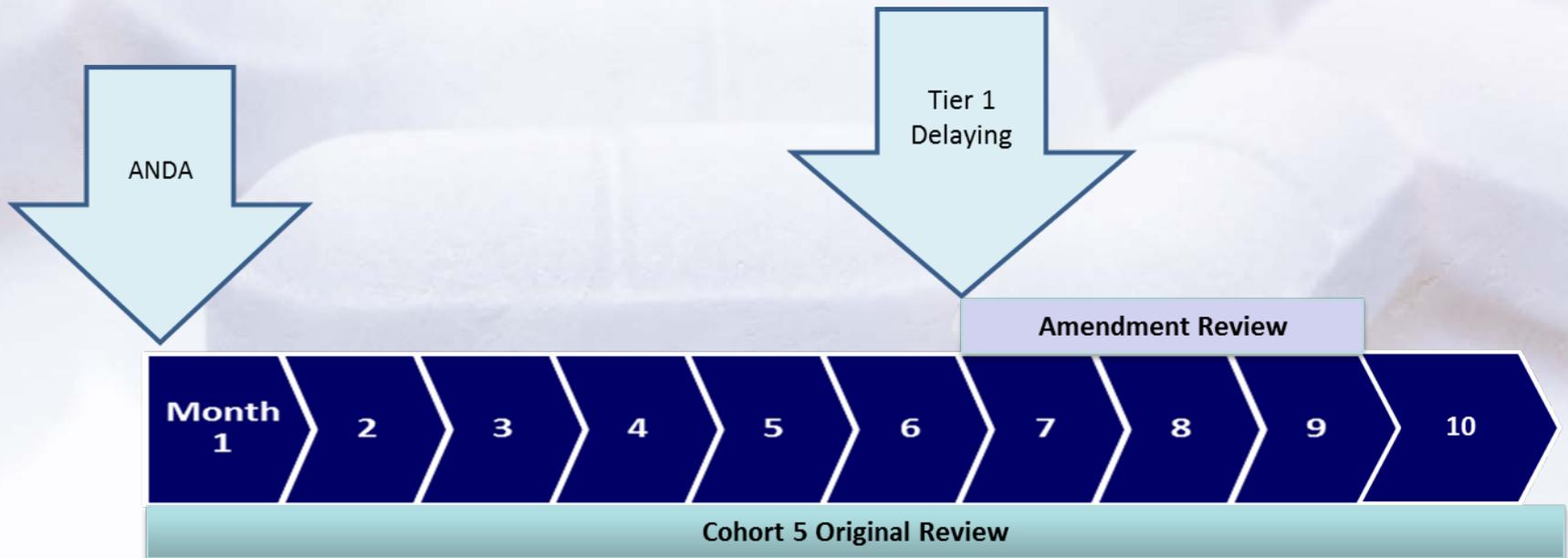
Example: Post-CR Amendments

A major amendment with a 10-month performance goal date submitted post-CR letter sets a new goal date for the application.



Example: Longest Goal Date Applies

A delaying amendment with a 3-month performance goal date submitted 4 months prior to the original goal date does not alter the review clock.



Application of Performance Goals

- Deferment
- Tentative Approvals
- Expedites

Deferment

- If an applicant submits a Tier 2 unsolicited amendment *after* FDA's issuance of a CR letter and *before* the applicant's submission of their CR amendment - review of the amendment will be deferred until the CR amendment is received
- A 12-month performance goal will apply to the application

Tentative Approvals

- Commitment Letter states that a request for final approval is an administrative amendment (no performance goal)
- If request for final approval contains substantive information that requires review
 - e.g., a change in validation procedures, a change in manufacturing facility
- FDA will classify the request as a Tier amendment subject to review goals

Expedites

- Certain submissions may be granted expedited review
- Amendments to expedited applications will be subject to the GDUFA performance goals
- If a submission has been granted expedited status, review may be completed before the goal date

Classification of Amendments

- General Policy
- Minor v. Unsolicited
- Minor v. ECD
- Overall Poor Quality

Classification: In General

- FDA will classify an amendment as major, minor, or ECD based on the resources required to review the submission
 - type
 - quantity
 - complexity of information to be reviewed

Classification: Minor v. Unsolicited

- Change from a minor to a major or unsolicited
- If an applicant's CR response amendment (minor amendment):
 - contains additional information unrelated to the CR deficiency (embedded) or
 - contains data beyond what was identified in the CR letter as necessary to correct the deficiency(ies)
- FDA will classify the submission as an unsolicited amendment and assign the appropriate performance goal

Classification: Minor v. ECD

- Applicants are requesting that their minor amendment be classified as ECD if they respond within 10 days
- Applicant's ability to respond in 10 days or less does not make a minor amendment an ECD
 - Classification based on FDA resources to review, not applicant turnaround time
- If a response to an ECD is not submitted within 10 business days, FDA will reissue the ECD as a minor deficiency in the next CR letter

Classification: Overall Poor Quality

- Concept introduced in 2001 guidance
- FDA classification in the CR letter:
 - If the CR Letter identifies:
 - multiple minor deficiencies of varying complexity
 - the review of which will require a substantial expenditure of FDA resources
 - akin to review of a major amendment
 - FDA will classify the response to the CR letter as a major amendment

Classification: Overall Poor Quality

- FDA changes classification upon review of the amendment
 - If a minor amendment CR response is of such poor quality that FDA cannot review without substantial resources
 - FDA will classify submission as a major amendment
- Change in classification will be at FDA's discretion
 - FDA may decide not to change the classification of a minor amendment of overall poor quality if it is Tier 3 amendment with no performance goal

Process

- Formatting recommendations for submission of amendments
- Process for Requests for Reconsideration

Recommendations: Submission Format

- A statement indicating whether the amendment is solicited or unsolicited
- The amendment classification or proposed classification based on the criteria provided in the guidance (major amendment, minor amendment, administrative amendment, delaying amendment or easily correctable deficiency)
- The tier classification (Tier 1, Tier 2 or Tier 3)
- A statement indicating whether the amendment contains any manufacturing or facilities changes
- A listing of the specific disciplines to review the amendment
- A statement indicating whether expedited review is requested

Request for Reconsideration

- Applicants need to seek reconsideration of a major amendment classification at the Division level
 - Classification of CR response
 - Change in amendment classification
- Once an applicant has sought reconsideration, the applicant can follow existing process for appeals above the Division level (See Guidance for Industry, Formal Dispute Resolution: Appeals Above the Division Level)

www.fda.gov/drugs/guidancecomplianceregulatoryinformation/guidances/default.htm

Request for Reconsideration

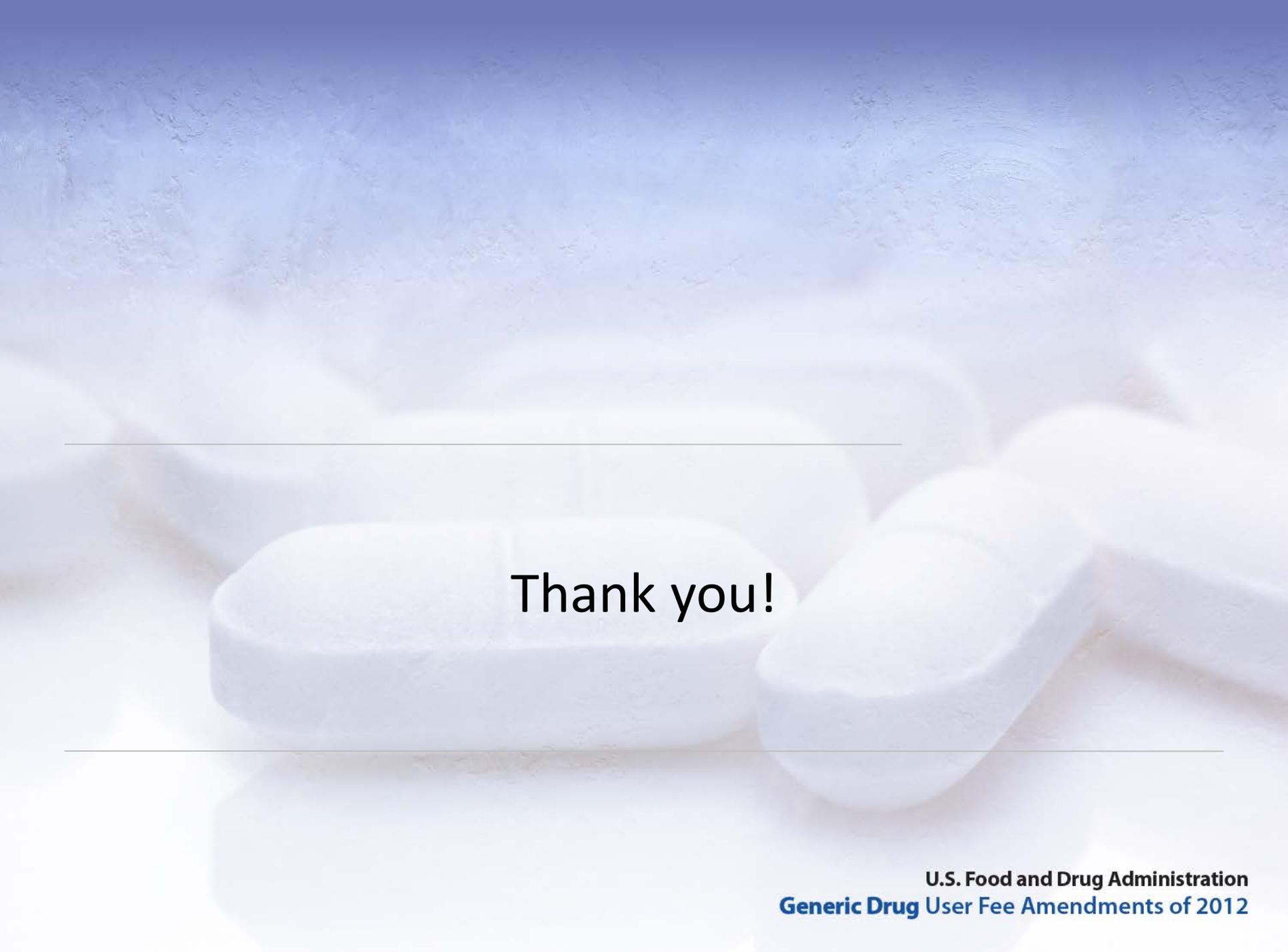
- CR Letter classification
 - Applicant submits a written request for a post-CR letter meeting within 10 business days from issuance of the CR letter
 - Applicant submits meeting materials including a comprehensive statement of why FDA should reconsider the classification
 - The Division issues a decision within 10 business days after the meeting
 - If request is successful before the applicant submits their amendment and a review goal is set, FDA will revise the classification and assign the appropriate performance goal upon submission
 - If request is successful but the amendment has been submitted and review has started, FDA will not change or alter the goal date for that amendment, but the amendment count will be adjusted

Request for Reconsideration

- Change in Classification
 - Applicant submits a written request for reconsideration within 10 days from issuance of amendment acknowledgment letter and provides information adequate to explain nature of the request (same criteria as for CR dispute)
 - The Division reviews the information submitted and determines whether the request for reconsideration will be granted or denied and will notify applicant within 10 business days
 - If request is successful, FDA will not change or alter the goal dates for that amendment, but the amendment count will be adjusted

Questions?

- For questions regarding the draft document contact:
 - (CDER) Elizabeth Giaquinto 240-402-7930
 - (CBER) Office of Communication, Outreach, and Development, 800-835-4709 or 240-402-7800.
- Please submit any comments on the guidance or this webinar to the public docket
 - FDA-2014-D-0902
 - Electronic comments may be submitted at www.regulations.gov



Thank you!
