Prescription Drug User Fee Act: Waivers, Exemptions, and Refunds – Oh My

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Topics

- Background Information
- Types of Fees
- Collection of Fees
- Waivers, Exemptions, Refunds
  - Different Types and Criteria
- Administrative Procedures

Background to PDUFA

- Food Drug and Cosmetic Act (FD&C Act)
  - Section 735 and 736
- PDUFA I enacted in 1992
- Must be reauthorized every 5 years
- Authorize FDA to collect fees

Reauthorized Every 5 Years

PDUFA	Fiscal Year	Act	Date Signed
I	1993-1997	Prescription Drug User Fee Act (PDUFA)	10/29/1992
II	1998-2002	Food and Drug Administration Modernization Act (FDAMA)	11/21/1997
III	2003-2007	Public Health Security and Bioterrorism Preparedness and Response Act (Bioterrorism Act)	6/12/2002
IV	2008-2012	Food and Drug Administration Amendment Act (FDAAA)	9/27/2007
V	2013-2017	Food and Drug Administration Safety and Innovation Act (FDASIA)	7/9/2012
VI	**2018-2022**	**Food and Drug Administration Reauthorization Act (FDARA)**	**8/18/2017**

Background to PDUFA

- Authorize FDA to collect fees for certain human drug and biological products

Center for Drug Evaluations and Research (CDER)	Center for Biologics Evaluation and Research (CBER)
New Drug Application (NDA) - 505(b)(1) & 505(b)(2)	
Biologics License Application (BLA) - 351(a)	

Type of Fees

Types of Fees

- PDUFA VI authorized two types of fees

Fee Type	% of Target Revenue for FY
Application	20%
Program	80%

- Target revenue amount set annually prior to the start of the new fiscal year
  - E.g. FY 2019 target revenue = $1,010,322,000 (~$1 Billion)
- FR Notice published in August

Application Fee

- Due upon submission of application
- FY 2019 Full Fee - $2,588,478
  - Application for which **clinical data** (other than bioavailability or bioequivalence studies) with respect to safety or efficacy are **required for approval**
- FY 2019 Half Fee - $1,294,239
  - Application for which **clinical data** with respect to safety or efficacy are **not required for approval**

Annual Program Fee

- Applied to each **approved** prescription drug product in an NDA/BLA
- **Annual fee**
- Payment due Oct. 1 of each fiscal year
- Based on published list of marketed prescription drug products
  - Orange Book
  - CDER Therapeutic Biologic Products List
  - CBER Billable Biologics List
- FY 2019 Program Fee = $309,915

Annual Program Fee

Approval Date	First Annual Program Fee Due
On or Before October 1, 2018	October 1, 2018 (FY2019)
After October 1, 2018	October 1, 2019 (FY2020) *Pass Until Next Fiscal Year*

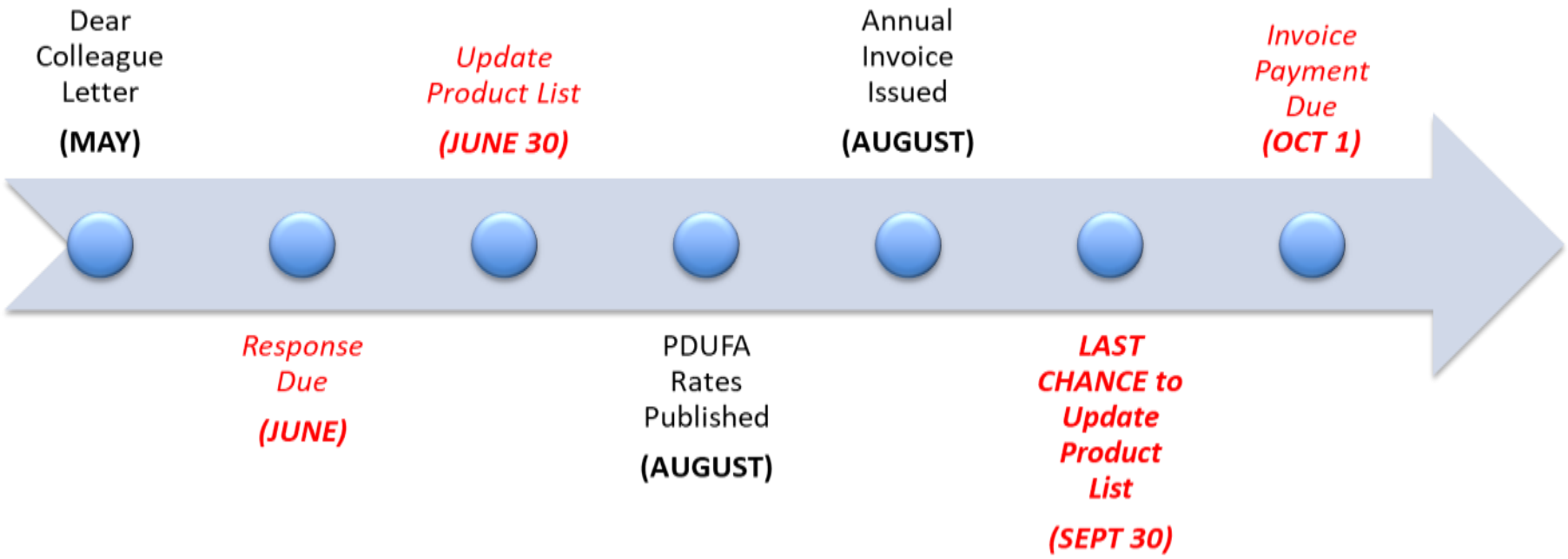
Annual Program Fee

- Excluded from program fee
  - Discontinued (no longer marketed)
  - Large Volume Parenteral (LVP)
  - Same Product as Another Product (only for NDAs)
    - Therapeutically Equivalent Drug Product in Orange Book
- Limited to 5 product per applications

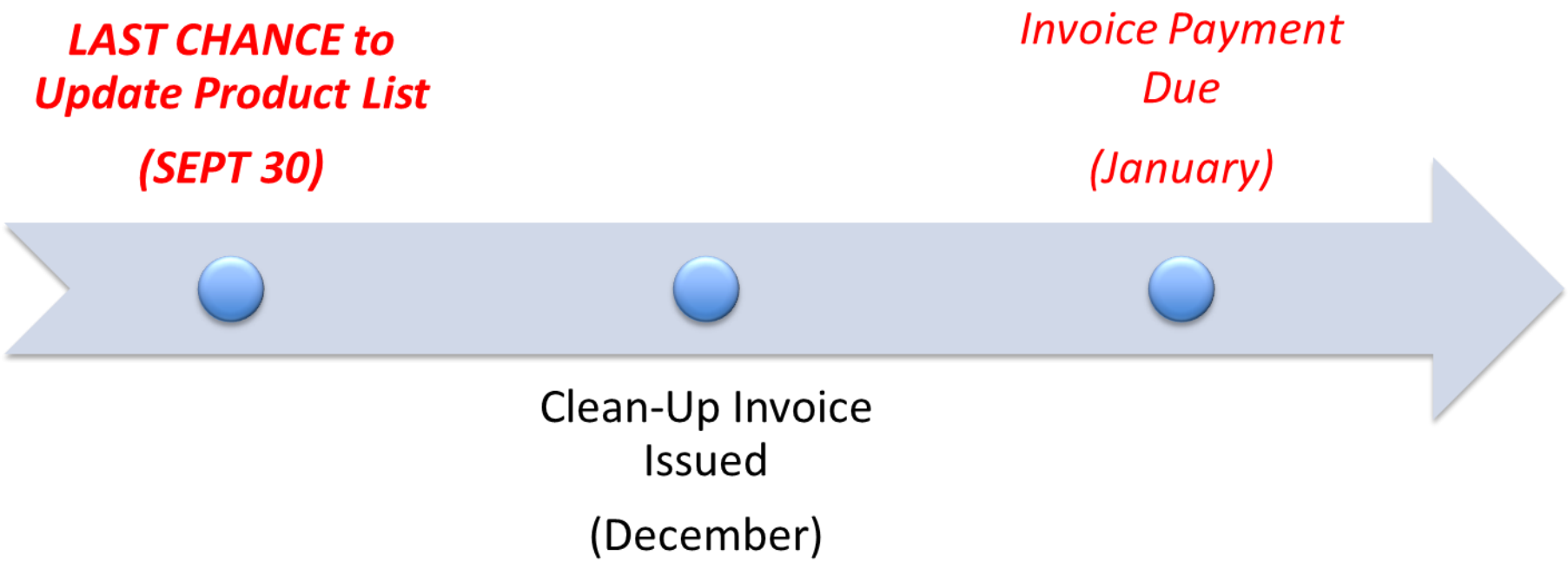
Collection of Annual Program Fee

- Invoices for annual program fees are assessed to applicant holders twice a year
  - Annual Billing Cycle: invoices are **issued in mid-August.** Fees are **due October 1st** of the Fiscal Year
  - Clean-Up Billing Cycle: invoices are **issued in mid-December.** Fees are **due in mid-January**

Annual Billing Timeline



Clean-Up Billing Timeline



Waivers

Exemptions

Refunds

Waiver Guidance

- New Draft Guidance – June 2018
  - Prescription Drug User Fee Act Waivers, Reductions, and Refunds for Drug and Biological Products
- Old Final Guidance – September 2011 (OUTDATED)
  - ~~User Fee Waivers, Reductions, and Refund for Drug and Biological Product~~

Orphan Exemptions

- Application fee exempt if:
  - Designated for a rare disease
  - Does not include an indication for other than a rare disease or condition
  - No written request needed
    - User Fee Cover Sheet, Form FDA 3397
    - Cover letter – brief statement

Orphan Exemptions

- Annual program fee exempt if:
  - Meets the public health waiver requirements
  - Must have < $50 million in gross worldwide revenue **(including affiliates)** during the previous year
  - Must submit a written request to FDA

Orphan Exemption - Summary

Fee Type	Prior Written Request	Orphan Designation	Financial Requirement	Payment Due
Application	No	Yes (but no other indication)	None	Once
Program	Yes	Yes	<$50 million (including affiliates)	Annual

Waivers

- Small Business
- Public Health
- Barrier-to-innovation (BTI)
  - President's Emergency Plan for AIDs Relief (PEPFAR)
  - Positron Emission Tomography (PET)

Small Business Waiver

- Applies ONLY to application fees
- Application fee waived if:
  - Applicant employs <500 employees, **including employees of affiliates**
  - Applicant does not have a drug product that has been approved under a human drug application and introduced or delivered into interstate commerce
  - Applicant **(and affiliates)** is submitting first human drug application

Small Business Waiver

- Expires after 1 year
- Fill out Small Business Waiver and Refund Request (Form FDA 3971)

Public Health

- Application and/or Program fee waived if:
  - Product protects the public health, AND
  - Limited financial resources (<$20 million), **including affiliates**

Public Health

- Considerations:
  - Significant improvement compared to other marketed products
  - Lack of treatment alternatives
  - Priority drug, fast track status, new molecular entity
  - Increased effectiveness in treatment, prevention, or diagnosis of a disease
  - Eliminate or substantially reduce a treatment-limiting drug reaction
  - Enhance patient adherence to treatment
  - Potential evidence of safety and effectiveness for a new or underserved subpopulation
  - Intended for the treatment of a serious or life-threatening condition
  - Address unmet medical needs
  - Orphan drug

Barrier-to-innovation

- Application and/or Program fee waived if:
  - Product or other products or technologies under development by the applicant are innovative, AND
  - Limited financial resources (<$20 million), **including affiliates**

Barrier-to-innovation

- Considerations:
  - Advanced “breakthrough” research, new, progressive methods, and/or forward thinking in the treatment or diagnosis of disease
  - Potential to be at the forefront of new medical technology
  - Unique or superior method for diagnosing, curing, mitigating, treating, or preventing a disease, or for affecting a structure or function of the body
  - Priority drug, fast track status, new molecular entity
  - Active IND under which evaluating a unique or superior method for diagnosing, curing, mitigating, treating, or preventing a disease, or for affecting a structure or function of the body
  - Recently received a Federal grant for innovation

PEPFAR Waiver

- President's Emergency Plan for AIDs Relief (PEPFAR)
- Barrier-to-innovation
- Application fee only

PEPFAR Waiver Guidance

- New Draft Guidance – June 2018
  - Prescription Drug User Fee Act Waiver for Fixed-Combination Antiretroviral Drugs for the President's Emergency Plan for AIDS Relief
- Old Final Guidance – February 2007 (OUTDATED)
  - ~~User Fee Waiver for FDC and Co-Packaged HIV Drugs for PEPFAR~~

PEPFAR Waiver – Application Fee

- Barrier-to-innovation criteria
  - Drug for treatment of HIV from **fixed dose guidance list**
  - Greater than $20 million in financial resources, other circumstances:
    - **Only tentative approval**
    - Available to PEPFAR countries at competitive prices

PEPFAR Waiver

- Fixed Dose Guidance List:
  - Attachment B – Fixed Dose Combination Co-Packaged Drug Products, and Single-Entity Versions of Previously Approved Antiretrovirals for Treatment of HIV (Final) October 2016
- FDA **may reevaluate** whether particular fixed-combinations remain innovative and may find that an application fee waiver is no longer needed.

PET Waiver

- Positron Emission Tomography (PET) drug
- Federal Register (FR) notice, 65 FR 12999 – March 10, 2000
- Barrier-to-innovation
- Application fee only

PET Waiver

Drug	Include Indication
FDG F 18 injection	for the identification of regions of abnormal glucose metabolism associated with foci of epileptic seizures
Ammonia N 13 injection	for evaluation of myocardial blood flow
Sodium fluoride F 18 injection	as a bone imaging agent to define areas of altered osteogenic activity

PET Waiver

- Barrier-to-innovation criteria
  - One of the three mentioned PET products including specific indications
  - Greater than $20 million in financial resources, other circumstances:
    - Waive market exclusivity

Waiver Summary

Waiver Type	Application Fee	Program Fee	Financial Requirement	Other Conditions
Small Business	Yes	No	None	• First application • <500 employee (including affiliates) • No approved drug being marketed
Public Health	Yes	Yes	<$20 million (including affiliates)	Protects public health
Barrier-to-innovation	Yes	Yes	<$20 million (including affiliates)	Innovative
PEPFAR	Yes	No	None	• Tentative approval only • Market to PEPFAR countries
PET	Yes	No	None	Waive market exclusivity

Administrative Procedures

Administrative Procedures

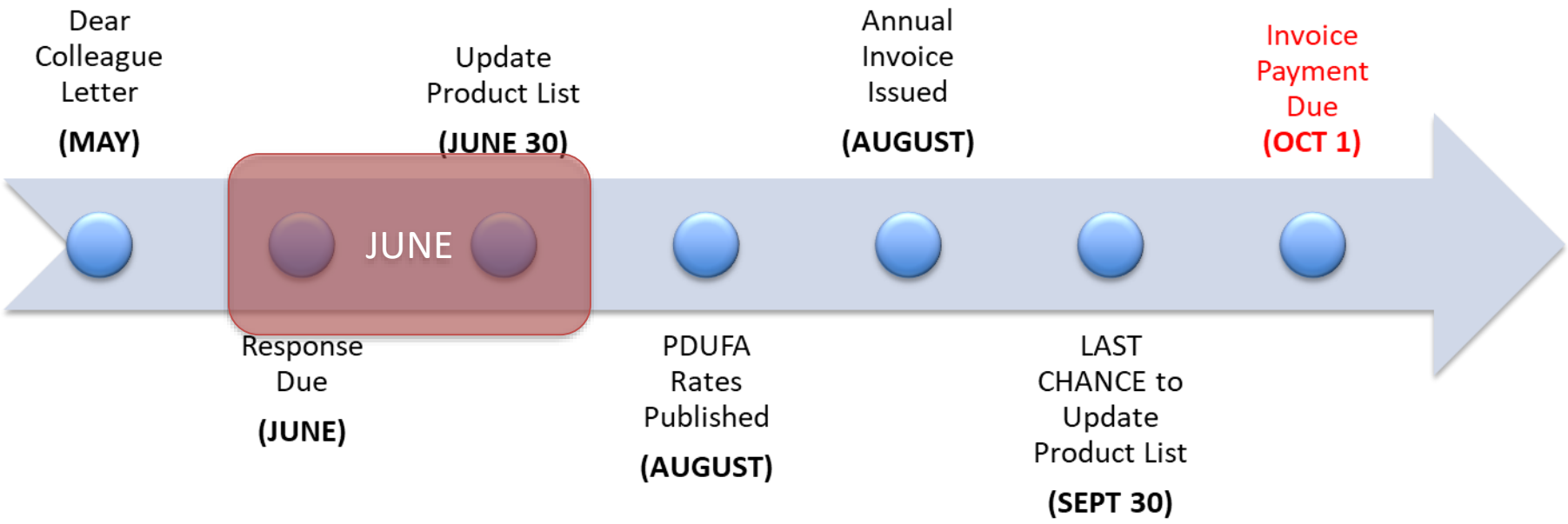
- When
- Where
- What

Administrative Procedures - When

- Submit 3-4 months in advance
  - Before submission of the Application
  - Annual program fees

Billing Cycle	Payment Due	Submit Request
Annual	October 1	June
Clean-Up	Mid-January	September

Administrative Procedures - When



Administrative Procedures - Where

- **Prefer firms email to:** CDERCollections@fda.hhs.gov
- Mailing Address available on PDUFA website

Administrative Procedures - What

- Applicant Information
- **Letter of Authorization** – if using an agent
- Application Information
- Type of Fee – Application or Program

Administrative Procedures - What

- Statutory Provision

Statute	Type
736(d)(1)(A)	Public Health
736(d)(1)(B)	Barrier-to-innovation
736(d)(1)(C)	Small Business
736(k)	Orphan

Administrative Procedures - What

- Demonstrate Eligibility
- Provide Rational Why
- List of Affiliates

Administrative Procedures - What

- Financial Documents for applicant and **affiliates**
  - Public Health and Barrier-to-innovation
    - Annual Financial Report or Other Reports (<$20 million)
  - Orphan (only for annul program fees)
    - Certification and Financial Documents (<$50 million)

Administrative Procedures - What

- Small Business
  - Fill out Small Business Form (Form FDA 3971)
  - Email subject line: Small Business Waiver Request – [*Applicant Name*]

Administrative Procedures - Reminder

- Exceptions for Junk and Spam Folder:
  1. CDERCollections@fda.hhs.gov
  2. DoNotReply@fda.hhs.gov
- Update Email Contact Information

Administrative Procedure - Extra

- Withdraw from sale notification for NDAs
  - Section 506I of the FDA&C Act
  - New Draft Guidance – January 2019
    - Marketing Status Notifications Under Section 506I of the Federal Food, Drug, and Cosmetic Act; Content and Format
  - Submit through the Electronic Submissions Gateway (ESG)
  - Prominently ID the submission: "ADMINISTRATIVE CHANGE / NOT AVAILABLE FOR SALE"

Reconsideration and Appeals

- Reconsiderations – Applicant disagrees with FDA's waiver decision
  - Submit within 30 calendar days of FDA letter
  - Reason why disagree and any additional information
  - Send to CDERCollections@fda.hhs.gov

Reconsideration and Appeals

- Appeals – Applicant disagrees with FDA's reconsideration decision
  - Submit within 30 calendar days of FDA letter
  - No new information or analyses
  - Send to CDERCollections@fda.hhs.gov and copy CDER Formal Dispute Resolution Project Manager at CDERFormalDisputeResolutionProgram@fda.hhs.gov

But, none of this matters…

…if written request not submitted on time!

To qualify, applicant must submit to FDA a written request for a user fee waiver or reduction not later than 180 calendar days after the fee is due.

Failure to Pay

- Failure to pay application fee
  - Submission considered incomplete and not accepted for filing
- Arrears for non payment of annual fees
  - All incoming submissions considered incomplete and not accepted for filing (for the applicant and its affiliates)
  - Financial penalties incurred
  - Delinquent debts reported to credit reporting agencies
  - Referred to debt collection agencies

Failure to Pay - Question

If my waiver request is pending do I have to pay my invoice?

- FDA does NOT grant deferrals of user fees based on pending waiver requests therefore all program fees should be paid with regard to pending request for a fee waiver.

Important Dates and Reminders

- June – Submit waiver request for program fees
- June 30 - Notify FDA to update product list (Orange Book, CDER/CBER BLA List)
- Sept. 30 – LAST CHANCE to update product list
- Oct. 1 – Annual Program Fee Due

Challenge Question # 1

Which waiver can only be used for application fees?

a) PEPFAR

b) Small business

c) Public health

d) PET

e) a, b, and d

Challenge Question # 2

Which waivers have a criteria for a financial limit of $20 million?

a) Small business

b) Public health

c) Barrier-to-innovation

d) b and c

e) All the above

Resources

- PDUFA Website
- Orange Book
- CDER Therapeutic Biologic Products List
- CBER Billable Biologics List
- Prescription Drug User Fee Act Waivers, Reductions, and Refunds for Drug and Biological Products (Draft) June 2018

Resources

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Contact Information

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