FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH
SMALL BUSINESS AND INDUSTRY ASSISTANCE

Priority Review Vouchers – General Information and Redemption

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Objectives

- Overview of FDA priority review voucher (PRV) programs
- Eligibility requirements
- Redemption of PRV
- Common questions and issues
- Resources and Contacts

Overview – PRV Program Types

Tropical Disease (TD)	Rare Pediatric Disease (RPD)	Medical Countermeasures (MCM)
Section 524 of the FD&C Act	Section 529 of the FD&C Act	Section 565A of the FD&C Act
• 2007 - Food and Drug Administration Amendment Act • 2014 - Adding Ebola to the FDA Priority Review Voucher Program Act • 2016 - Adding Zika Virus to the FDA Priority Review Voucher Program Act	• 2012 - Food and Drug Administration Safety and Innovation Act • 2016 - Advancing Hope Act • 2016 - 21st Century Cures Act	• 2016 - 21st Century Cures Act

Overview – PRV Purpose

- Tropical Disease – designed to encourage development of new drug and biological products for prevention and treatment of certain tropical diseases affecting millions of people throughout the world.
- Rare Pediatric Disease – designed to encourage development of new drug and biological products that prevent or treat serious or life threatening rare pediatric diseases in the US.
- Medical Countermeasures – designed to encourage development of new drug and biological products to prevent or treat harm from chemical, biological, radiologic, and nuclear (CBRN) agents.

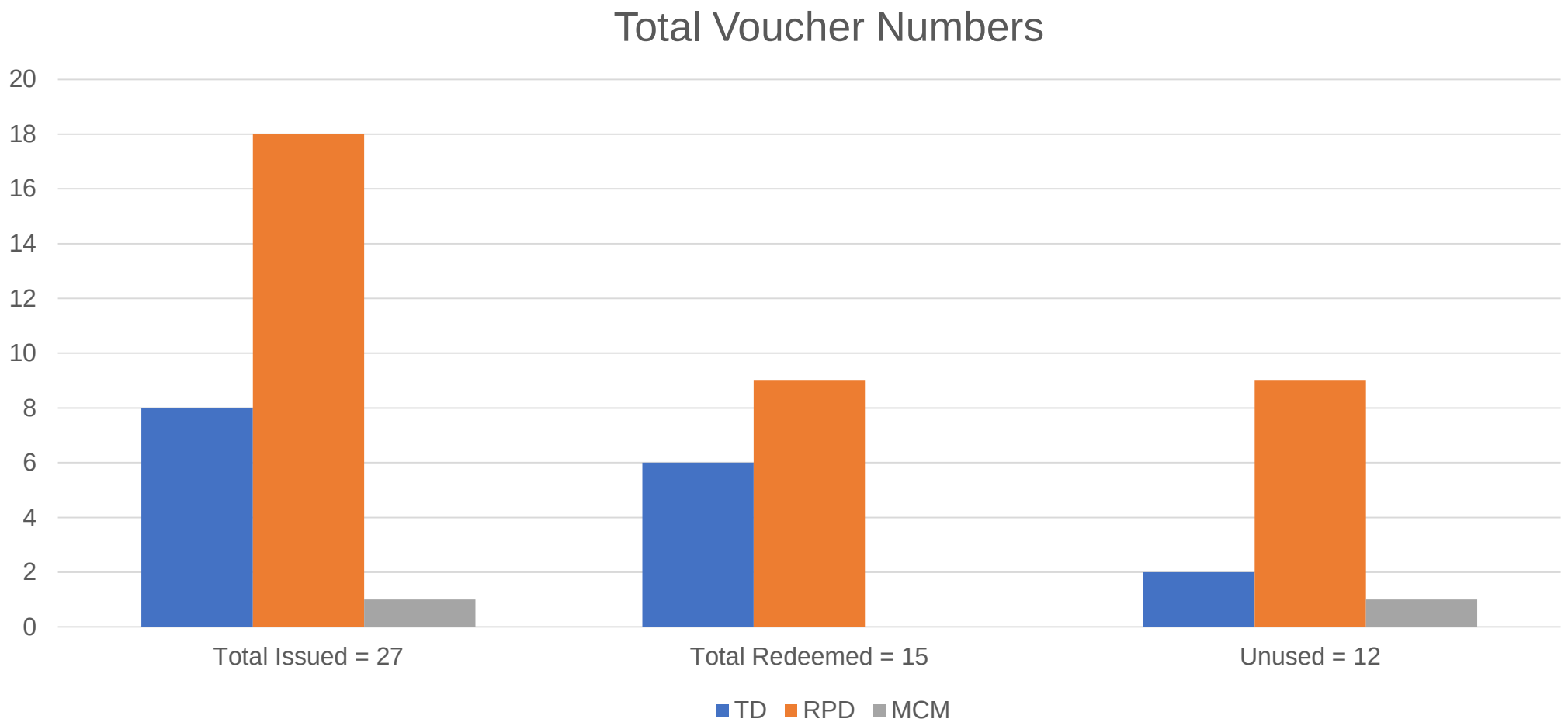
Overview – What Is a PRV

- Awarded by the FDA when qualifying applications are approved
  - Tropical Disease Application
  - Rare Pediatric Disease Application
  - Medical Countermeasure Application

- Entitles an application to priority review

Standard Review	Priority Review
10 months of the 60 day filing date	6 months of the 60 day filing date

Overview – PRV Numbers



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Eligibility – Common Requirements

1. Human drug application
2. Application determined by FDA to be eligible for priority review
3. Application approved by the FDA after the date of enactment of the authorizing statutes
   - TD – After 9/27/2007
   - RPD – After 7/9/2012
   - MCM – After 12/13/2016
4. Application contains no active ingredient that has been previously approved

Eligibility – Tropical Disease

Application is for prevention or treatment of a tropical disease

Designated by statute:

- Tuberculosis
- Malaria
- Blinding trachoma
- Buruli Ulcer
- Cholera
- Dengue/dengue haemorrhagic fever
- Dracunculiasis (guinea-worm disease)
- Fascioliasis
- Human African trypanosomiasis
- Leishmaniasis
- Leprosy
- Lymphatic filariasis
- Onchocerciasis
- Schistosomiasis
- Soil transmitted helmithiasis
- Yaws
- Filovirus diseases
- Zika virus disease

Designated by FDA order:

- Chagas
- Neurocysticercosis
- Chikungunya virus disease
- Cryptococcal meningitis
- Lassa fever
- Rabies

Eligibility – Rare Pediatric Disease

1. Application is for the prevention or treatment of a rare pediatric disease. Rare pediatric disease means it is
   - A serious or life threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years and
   - A rare disease or condition that affects fewer than 200,000 persons in the US.
2. Application relies on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population.
3. Does not seek approval for an adult indication in the original rare pediatric disease application

Eligibility – Medical Countermeasure

Application is for a drug product intended

- For use to prevent or treat harm from a CBRN agent identified as a material threat under section 319F-2(e)(2)(A)(ii) of the PHS Act; or
- To mitigate, prevent, or treat harm from a condition that may result in adverse health consequences or death and may be caused by administering a drug or biological product against such agent.

Section 319F-2(e)(2)(A)(ii) of the PHS Act provides that Secretary of Homeland Security, in consultation with other Agencies, shall determine such CBRN agents that present a material threat against the US population sufficient to affect national security.

Eligibility – Medical Countermeasure

DHHS, in its annual *Public Health Emergency Medical Countermeasures Enterprise* (PHEMCE) *Strategy and Implementation Plan* (here), publishes a list of high-priority threats including those determined by the Homeland Security Secretary.

Box 1: PHEMCE High-Priority Threats

The PHEMCE will continue to address MCM needs to protect against high-priority threats for which the Secretary of Homeland Security made a determination pose a material threat sufficient to affect national security or PHEMCE leadership determines to have the potential to threaten national health security. This year, the PHEMCE added three chemical agents (chlorine, phosgene, and vesicants); otherwise, the high-priority threats are unchanged from those listed in the *2016 PHEMCE SIP*. The PHEMCE high-priority threats are (in alphabetical order by threat area):

Biological Threats
- *Bacillus anthracis* (anthrax)* and Multi-drug resistant *B. anthracis* (MDR anthrax)*
- *Burkholderia mallei* (glanders)* and *Burkholderia pseudomallei* (melioidosis)*
- *Clostridium botulinum* toxin (botulism)*
- Ebola virus (Ebola hemorrhagic fever)*
- Emerging infectious diseases[4]
- *Francisella tularensis* (tularemia)*
- Marburg virus (Marburg hemorrhagic fever)*
- Pandemic influenza
- *Rickettsia prowazekii* (typhus)*
- *Variola* virus (smallpox)*
- *Yersinia pestis* (plague)*

Chemical Threats
- Acetylcholinesterase inhibitor nerve agents*
- Chlorine[5]
- Cyanide salts (potassium and sodium cyanide)*
- Hydrogen cyanide*
- Phosgene[5]
- Vesicants*

Radiological* and Nuclear* Threats

(*) indicates threats identified under the following authorities related to MCMs: (1) emergency use authorities that rely on section 564(b)(1)(D) of the Federal Food, Drug, and Cosmetic Act (FD&C Act); (2) priority review vouchers PRVs) under section 565A of the FD&C Act;[6] and, (3) procurements of security countermeasures under section 319F-2 of the PHS Act.

Eligibility – Issuance of PRV

PRV means a voucher issued by the Secretary for an eligible application (TD/RPD/MCM) that entitles the holder of such voucher to priority review of a single human drug application submitted under 505(b)(1) or section 351(a) of the PHS Act, after the date of approval of such application.

Cannot be issued prior to approval even if the application meets all the requirements at the time of submission.

Eligibility – Issuance of PRV

- Issuance of a MCM PRV to SIGA Technologies, Inc. for approval of NDA 208627 for TPOXX (tecovirimat) used to treat patients with smallpox disease.
- Issued within an approval letter for the NDA.
- NDA/BLA number is used as tracking number for the PRV.
- Contains additional instructions

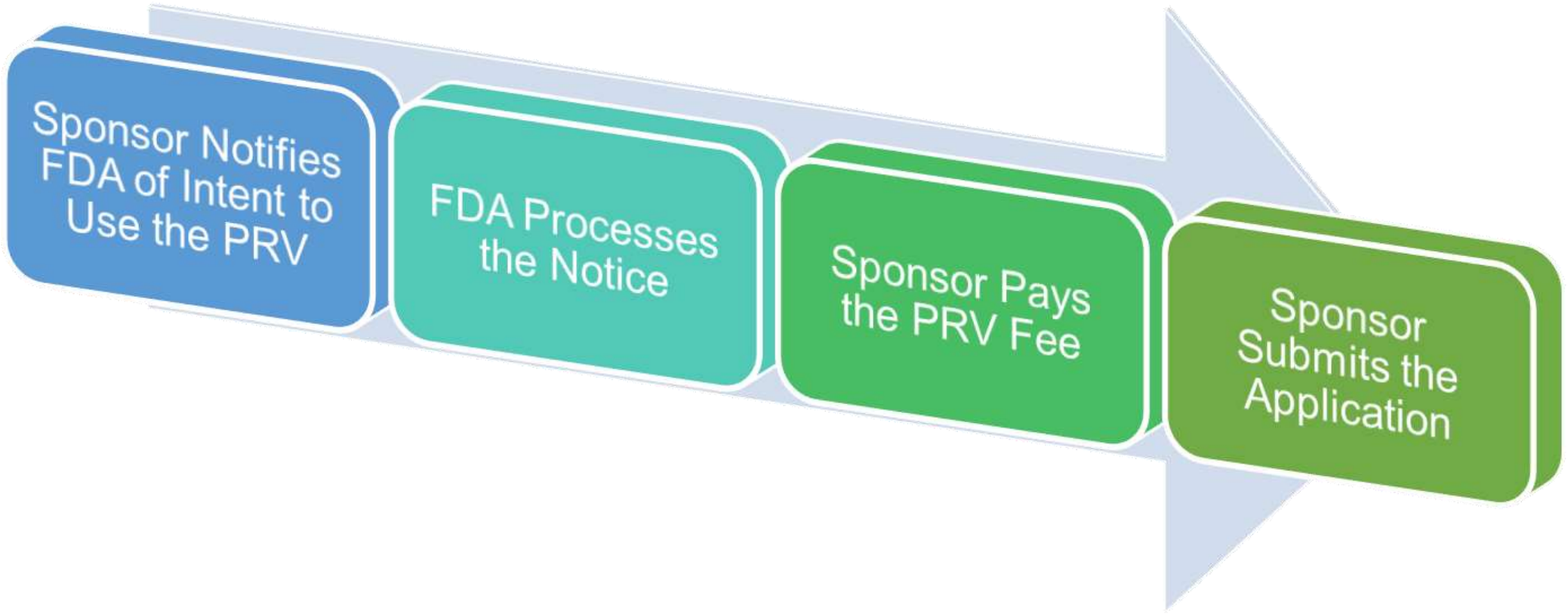
MATERIAL THREAT MEDICAL COUNTERMEASURE PRIORITY REVIEW VOUCHER

We also inform you that you have been granted a material threat medical countermeasure priority review voucher (PRV), as provided under section 565A of the FDCA. This PRV has been assigned a tracking number, PRV NDA 208627. All correspondences related to this PRV should refer to this tracking number.

This PRV entitles you to designate a single human drug application submitted under section 505(b)(1) of the FDCA or a single biologic application submitted under section 351 of the Public Health Service Act as qualifying for a priority review. Such an application would not have to meet any other requirements for a priority review. This PRV may be transferred by you to another sponsor of a human drug or biologic application. If the PRV is transferred, the sponsor to whom the PRV has been transferred should include a copy of this letter (which will be posted on our website as are all approval letters) and proof that the PRV was transferred. When redeeming this PRV, you should refer to this letter as an official record of the voucher. The sponsor who redeems the PRV must notify FDA of its intent to submit an application with a PRV at least 90 days before submission of the application, and must include the date the sponsor intends to submit the application.

FDA has published a draft guidance, *Material Threat Medical Countermeasure Priority Review Vouchers,* at https://www.fda.gov/downloads/regulatoryinformation/guidances/ucm592548.pdf. This guidance, when finalized, will represent the current thinking of the FDA on this topic.

Redemption – Procedures



Redemption – Notification of Intent

A sponsor redeeming the PRV must notify FDA of its intent to submit a human drug application using a PRV at least 90 days prior to the submission of the application.

- Submit notice to the NDA/BLA and/or IND
- Notify the RPM for the review division responsible for review of your drug product
- Notify the user fee staff at CDERCollections@fda.hhs.gov or CBERPDUFAStaff@fda.hhs.gov

The contents of the notice should:

- ✓ Indicate the application and product for which to apply the PRV
- ✓ Indicate date the sponsor intents to submit the application
- ✓ Provide the applicant name for the intended application and the PRV holder name
- ✓ Provide complete records of transfers, if any

Redemption – FDA Process for RPD

Redemption – FDA Process for TD and MCM

Redemption – Payment of PRV Fee

When are PRV fees due?

- Rare Pediatric Disease PRV: Fees are due upon notification of intent

- Tropical Disease and Medical Countermeasure PRV: Fees are due upon submission of the application using the PRV

Redemption – PRV Fees

- FDA sets PRV fees for the next fiscal year and publishes FR notices generally in September prior to the start of the next fiscal year.
- PRV fees are published in the FR for each PRV program; however, the fee amounts are identical among the three programs.
- FY 2019 priority review fee – $2,457,140

Redemption – Submission of Application

Once an application using the PRV has been submitted and the applicable fees paid, the PRV is used.

- Application may not be submitted prior to the elapse of the 90 day notice period.
- If PRV fees, or application fees have not yet been paid, the application is considered incomplete
- Prior to submission of the application, the applicant may withdraw the notice of intent.

Common Questions

Q1 When can a PRV be used? A sponsor must notify the FDA 90 days in advance of submitting a human drug application that is to be used with the PRV.

Q2 Can a PRV be used for a supplement? No. The PRV statutes describe a priority review with respect to a human drug application as defined in section 756(1) of the FD&C Act that explicitly excludes supplements.

Q3 Can a PRV be transferred? Yes, it can be transferred unlimited times, including by sale. Document the transfer with letter from former owner and a letter from new owner acknowledging the transfer. A PRV cannot be redeemed unless a complete record of transfer is made available to the FDA.

Q4 Will use of a PRV guarantee that FDA will complete the review and approve a human drug application within 6 months? No. the PRV statutes define priority review as FDA review and action taken not later than 6 months after FDA receipt as described in the PDUFA commitment letter review goals. The goals for priority review are 90% in 6 months of the 60 day filing date. FDA commits to take action within 8 months of application submission in 90% of cases. An FDA action can mean approval or complete response letter.

Common Questions

Q5 Will a resubmission to a complete response receive priority review? No. Substantively, review goals are the same between standard and priority reviews for resubmissions.

Q6 What fees apply when using a PRV? The sponsor of the application using the PRV must pay a priority review fee in addition to the fees required under PDUFA. The priority review fee schedule is published in the FR for each fiscal year prior to the start of such fiscal year. The PRV fee is assessed for the fiscal year that the application using the PRV is to be submitted.

Q7 When does the sponsor pay the PRV fee?

- RPD: when the sponsor notifies the FDA of the intent to use the PRV
- TD and MCM: when the sponsor submits the application using the PRV

Q8 Can PRV fees be waived or refunded? No. The PRV statutes prohibit FDA from granting waivers, exemptions, reductions, or refunds of any fees due under the statutes.

Common Questions

Q9 Are there differences that may impact voucher holders for vouchers issued among the different PRV programs?

- ❖Tropical Disease and Medical Countermeasures:
  - PRV fees are due and must be paid upon submission of the application using the PRV
- ❖Rare Pediatric Disease:
  - PRV fees are due and must be paid upon notice of intent to use the PRV
  - a person who receives the transfer of a voucher shall notify the FDA of the change in ownership within 30 days of the transfer
  - the voucher may be revoked if the approved RPD product is not marketed within 365 day after the date of approval
  - sponsor of the approved RPD product application must submit a report to the FDA no later than 5 years after approval

References - Legislations

- Priority Review to Encourage Treatments for Tropical Diseases
  Section 524 of the FD&C Act (21 U.S.C. § 360n)
- Priority Review to Encourage Treatments for Rare Pediatric Diseases
  Section 529 of the FD&C Act (21 U.S.C § 360ff)
- Priority Review to Encourage Treatments for Agents That Present National Security Threats
  Section 565A of the FD&C Act (21U.S.C. § 360bbb-4a)

References - Guidances

- *Tropical Disease Priority Review Vouchers, Guidance for Industry* (here)
- *Rare Pediatric Disease Priority Review Vouchers, Draft Guidance for Industry* (here)
- *Material Threat Medical Countermeasure Priority Review Vouchers, Draft Guidance for Industry* (here)

References - Contacts

- CDER User Fee Staff (CDERCollections@fda.hhs.gov) for questions concerning user fee redemption of vouchers for a CDER regulated products.
- CBER User Fee Staff (CBERPDUFAStaff@fda.hhs.gov) for questions concerning user fee redemption of vouchers for CBER regulated products.
- CDER Office of New Drugs review divisions (here) for questions concerning drug development and qualification for CDER regulated TD/RPD/MCM applications.
- CBER offices and review divisions (here) for questions concerning drug development and qualification for CBER regulated TD/RPD/MCM applications. For CBER regulated MCMs contact (CBEREUA@fda.hhs.gov).
- Office of Orphan Product Development (Orphan@fda.hhs.gov) for questions concerning orphan designation and rare pediatric disease designation.
- Office of Counterterrorism and Emerging Threats (AskMCMi@fda.hhs.gov) for questions on medical countermeasure products regulated by CDER.

Challenge Question #1

True or False

An application for a product that contains a different salt form of an active ingredient that was previously approved in a 505(b)(1) application is eligible to receive a priority review voucher.

Challenge Question #2

A priority review voucher

a) Commits FDA to a review time of 6 months from date of submission

b) Guarantees application approval within 6 months of date of receipt

c) Neither guarantees a 6 month review time nor guarantees an application approval within 6 months of receipt

d) May be used with a supplement

Challenge Question #3

True or False

A sponsor submits a notification of intent to use a rare pediatric disease PRV, receives an invoice, and pays the PRV fees due. Prior to submission of the intended application, the sponsor decides to withdraw the notification of intent. Since the PRV is not being used, FDA may issue a refund of the PRV fees paid.

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