Principles of Pharmaceutical Regulations
June 23, 2016
Poll

Please take a moment to answer the open poll question.

What is your affiliation?

• Federal Government
• State Government
• Local (City or County) Government
• Other
Introduction of moderators

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Centers for Disease Control and Prevention
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@gburel

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Introduction of speakers

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Chairman, Pharmaceutical Cargo Security Coalition (PCSC)

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Associate Director for Science, Division of Strategic National Stockpile, CDC
Agenda

• Welcome
• Introduction and Overview
• U.S. Regulation of Pharmaceuticals
• Pharmaceutical Supply Chain Risk Mitigation Programs
• Regulatory issues affecting the Strategic National Stockpile (SNS)
• Discussion
• Recap and Closing
Objectives of this session

• Understand the groups charged with regulating the pharmaceutical supply chain.

• Understand how to work with these groups during times of crisis.

• Understand threats to the supply chain.

• Understand supply chain protection and mitigation programs in place.

• Understand emergency use authorizations (EUAs), investigational new drug applications (INDs) and emergency use instructions (EUIs).

• Understand regulatory processes related to SNS products.
U.S. Regulation of Pharmaceuticals
Poll

Please take a moment to answer the open poll question.

How familiar are you with the process by which prescription drugs are regulated in the U.S.?

• Very familiar
• Somewhat familiar
• Not familiar
How are prescription drugs regulated?

• State and Federal Legislation
  - Passed by legislature, signed into law by executive

• Key Statutes
  - Federal Food, Drug & Cosmetic Act (FDCA)
  - Public Health Service Act (PHSA)
  - Controlled Substances Act (CSA)
How are prescription drugs regulated?

• Key Policies and Regulations
  - Code of federal regulations
  - Guidance documents
  - Enforcement decisions

• Key Agencies
  - Food & Drug Administration (FDA)
  - Drug Enforcement Agency (DEA)
  - State boards of pharmacies (BOPs)
Poll

Please take a moment to answer the open poll question.

Does your organization have a relationship with your state’s board of pharmacy in place?

• Yes
• No
• Uncertain
• Not applicable
Overview of topics

• Key Laws and Regulations: Drug Development to Approval
  - Clinical trials
  - FDA submission and review

• Key Laws and Regulations: Post-Approval Activities
  - Current good manufacturing practices
    • Cold chain requirements
  - Post-marketing safety surveillance
  - Supply chain security
  - Special topics
    • Controlled substances
    • State oversight
Lengthy, costly, and uncertain: drug development

From drug discovery through FDA approval, developing a new medicine on average takes 10 to 15 years and costs $2.6 billion.* Less than 12% of the candidate medicines that make it into phase I clinical trials are approved by the FDA.


*The average R&D cost required to bring a new FDA-approved medicine to patients is estimated to be $2.6 billion over the past decade (in 2013 dollars), including the cost of the many potential medicines that do not make it through to FDA approval.

Source: PhRMA adaptation based on DiMasi JA, et al.; Tufts CSDD; FDA®
Clinical trials

https://www.youtube.com/watch?v=6B5S3-nTdD4
1. NDA/BLA Application
2. Application Reviewed
3. Drug Labeling
4. Facility Inspection
5. FDA Approval
Post-market activities

• Current Good Manufacturing Practices
  - Inspections
  - Cold chain considerations

• Post-Marketing Safety Surveillance and Reporting
  - FDA Adverse Event Reporting System (FAERS)
  - FDA’s MedWatch

• Supply Chain Security
  - Serialization
  - Reporting illegitimate products
Special topics

• **Controlled Substances**
  - Scheduling
  - DEA Oversight

• **State Regulations**
  - Licensure of wholesale distributors and pharmacies
  - Generic substitution
  - Compounding
  - Pharmaceutical disposal
Pharmaceutical Supply Chain Risk Mitigation Programs
Getting pharmaceuticals from plant to palate

Example - Opioids

Raw material Supplier: Tasmania/Spain
Manufacturer: Rhode Island/North Carolina
Wholesaler: McKesson, Cardinal, ABC
Retailer: CVS/Walgreens

YOU
Why pharmaceutical supply chain vulnerabilities have risen

1. “Just in time” or “lean” approaches
2. Contracted/outsourced manufacturing
3. Contracted/outsourced distribution
4. De-centralized points of distribution
5. Multiple subcontracting of logistical services
6. Sophistication of organized criminal cargo theft/counterfeiting groups
7. Value of large scale pharmaceutical shipments
8. Increase in illicit wholesale market opportunities
Product security

• Based on UPS’ Seventh Annual Pain in the (Supply) Chain Survey – Embracing Risk:
  – 46% of respondents cite product security as a top supply chain concern
  – 40% cite product damage or spoilage as a top supply chain concern
  – 48% report that counterfeiter sophistication is growing faster than countermeasures
  – 40% report that poor supply chain visibility and too many supply chain hand-offs are a problem
Poll

Please take a moment to answer the open poll question.

What do you think is the most common disruption to the supply chain?

• Theft
• Counterfeiting
• Failed hand-off/transfer of goods
• Unsure
Pharmaceutical thefts

• Breakdown of pharmaceutical events by type of event, based on research from FreightWatch International:
  – 50% pilferage
  – 38% theft of a full truckload
  – 4% facility theft
  – 4% fictitious pick-up
  – 4% hijacking
Progress against pharmaceutical cargo theft

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<th>Average Value of Loss</th>
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<td>47</td>
<td>$4,200,000</td>
</tr>
<tr>
<td>2011</td>
<td>36</td>
<td>$585,000</td>
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<tr>
<td>2015</td>
<td>14</td>
<td>$225,000</td>
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<tr>
<td>2016</td>
<td>1 (surgical packs – Canada)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2 (FTL pilferages)</td>
<td></td>
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Within first 6 months shipment recovery rates less than 35%

Within first 6 months shipment recovery rates nearing 60%
How do we reduce the rate of disruption/theft?

Everybody else -

Not so much...
Reducing the rate of disruption/threat

What you can do:

• **Know who you are doing business with**
  - Suppliers, last-mile carriers, freight-forwarders, airlines, warehousemen, 3PL’s, cross-docks...
  - “Vet” as many people that come in contact with the pharmaceutical products you work with as possible

• **Know where your goods are coming from – how they are getting to you**
  - Highway routes and metropolitan areas traversed
  - Airport/seaport cargo terminals
  - Interim warehouse storage
Reducing the rate of disruption/theft

- Conduct risk assessments of facilities that house your goods
  - Assess physical security of facilities, to include warehouse and shipping/receiving areas
    - Personnel access
    - Electronic surveillance
    - Security plans/programs

- Make investments in technology
  - GPS Tracking
  - Anti-theft and sophisticated tamper evident technology
## Alarm Log

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<th>Time</th>
<th>Address</th>
<th>Coordinate [lat - long]</th>
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Reducing the rate of disruption/theft

- Participate in educational seminars and conferences
  - Pharmaceutical Cargo Security Coalition (PCSC) Training Seminars
  - HDMA sponsored seminars
  - Healthcare Ready webinars
  - Law enforcement seminars

- Share intelligence relative to cargo theft incidents
  - PCSC Alerts
  - BSI, Freightwatch, IJET, etc...
  - Transportation Security Council Alerts
Pharmaceutical cargo security coalition (PCSC)

- Shares supply chain security intelligence
- Provides supply chain security education to the membership & those that support the pharmaceutical industry
- Acts as a law enforcement liaison
- Acts as a pharma industry reference
- “Linking” organization – providing industry/vendor contacts
- Statistical record keeper
Takeaways

Remember, it comes down to two things:

- Familiarity
- Visibility
Thank You

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Chairman – Pharmaceutical Supply Chain Security Coalition (PCSC)

Purdue Pharma LP

Supply Chain Security

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Emergency Use Authorizations and Investigational New Drugs
Federal Food, Drug, and Cosmetic Act

- The United States Federal Food, Drug, and Cosmetic Act (FD&C Act), is a set of laws passed by Congress in 1938 (and subsequently amended) giving authority to the U.S. Food and Drug Administration (FDA) to oversee the safety of food, drugs, cosmetics, and other products.

- Adulterated - differs from the standard of strength, quality, or purity

- Misbranded - changes to labeling, packaging, wording, information provided
Poll

How familiar are you with the investigational new drug application (IND) process?

- Very familiar
- Somewhat familiar
- Not familiar
Regulatory mechanisms must be in place before product can be released from SNS.
Need for Regulatory Mechanisms

- FDA is responsible for protecting the health of the public by assuring the safety, efficacy and security of drugs, biologics and medical devices.

- During an event when SNS assets are deployed, regulations still apply. Products must be:
  - FDA approved, or;
  - Used under an authorized regulatory mechanism.

- Many products in the SNS are not FDA approved or are FDA approved but are being used outside of the manufacturer’s approved indication.
What is an IND?

- IND = Investigational New Drug Application
- Permits distribution of a drug during an investigational period
- Broadly, refers to a body of regulations that guide the administration of an investigational drug (Found in 21 CFR 312)

- Three basic constituents
  - Informed consent
  - Protocol review (IRB)
  - Outcome collection (safety and efficacy)
Why is an IND needed?

- The use of an unapproved product
- The use of an approved product for a new, unapproved use
- Disease
  - Occurs infrequently (e.g., Anthrax) or
  - No longer occurs naturally to be studied (e.g. Smallpox)
  - Unethical to perform studies in humans
Drug Development Overview

Animal Studies

IND

Phase I
Tens
Safety trials

Phase 2
Hundreds
Safety/efficacy trials

Phase 3
Thousands
Safety/efficacy trials

FDA

IND

IND

NDA
CDC IND Protocols

- For SNS assets, CDC has IND protocols in place

- Protocols have been:
  - Developed by CDC
  - Reviewed by FDA
  - Submitted to IRB

- Protocols include
  - Scientific rationale
  - Details how to use the product
  - Consent forms
CDC Responsibilities

- Sponsor of IND
  - Supply protocol and related documents
  - IRB Approval
- Supply drug/biologic/device
- Report to FDA
State/Local Responsibilities

- Local Investigators
- Product Distribution
- Product Dispensing/Administration
  - Tracking (drug, lot numbers)
- Informed consent forms
- Information for Recipients
- Adverse Event Reporting/Monitoring
- Recordkeeping
MCM-Related Counterterrorism Legislation

  - Established final rule on animal models when human studies not ethical/feasible
  - Addressed accelerated approval of priority MCMs
  - Codified Strategic National Stockpile
MCM-Related Counterterrorism Legislation

  - Support development and procurement of MCMs
  - FDA authority to issue Emergency Use Authorizations
    - Gave FDA the legal authority to make certain types of drugs, biologics, and devices available in CBRN emergency situations
    - May be used for products that are unapproved (e.g., investigational) or that are approved but need to be used outside of their approved indication (e.g., a new age group) for the emergency response
Poll

How familiar are you with emergency use authorizations (EUAs)?

• Very familiar
• Somewhat familiar
• Not familiar
Why EUA?

- IND lessons learned from the 2001 anthrax
- IRB requirements not practicable during a rapidly progressive public health emergency
- Informed consent process may limit public health’s ability to respond and contain the disease/outbreak
EUA Background: Scope

**Types of Products:**
- Drugs
- Biologics
- Medical Devices

**Product Classification:**
- Unapproved product
- Unapproved use of an approved product
EUA vs. IND: The Objective

Emergency Use Authorization (EUA):
- Delivery of medical products for treatment/prophylaxis of the affected population in an emergency

Investigational New Drug Application (IND):
- Assess the safety of a medical product and assure human subject protection in a clinical trial
<table>
<thead>
<tr>
<th>Regulatory Requirement</th>
<th>Emergency Use Authorization (EUA)</th>
<th>Investigational Protocols (IND)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Institutional Review Board</td>
<td>Not Required</td>
<td>Required 21 CFR part 56</td>
</tr>
<tr>
<td>Written/Witnessed Informed Consent</td>
<td>Not Required</td>
<td>Required 21 CFR part 50</td>
</tr>
<tr>
<td>Protocol Training</td>
<td>Not Required</td>
<td>Required</td>
</tr>
<tr>
<td>Adverse Event Monitoring/Reporting</td>
<td>Required</td>
<td>Required</td>
</tr>
<tr>
<td>Recordkeeping/Access</td>
<td>Required for manufacturers; may be required for others</td>
<td>Required</td>
</tr>
<tr>
<td>Duration</td>
<td>Circumstances justifying EUA no longer exist or there is a change in the product’s approval status</td>
<td>Length of clinical trial</td>
</tr>
</tbody>
</table>
MCM-Related Counterterrorism Legislation

- Public Readiness and Emergency Preparedness Act of 2005 (PREP Act)
  - Authorizes HHS Secretary to issue a declaration (PREP Act declaration) that provides immunity from tort liability for claims of loss by administration or use of MCMs to diseases, threats, and conditions determined to constitute a present or credible risk of future public health emergency to entities/individuals involved in: development, manufacture, testing, distribution, administration, and use of such MCMs.
MCM-Related Counterterrorism Legislation

  - Does not cover willful misconduct
  - Declaration is different from other emergency declarations
  - Authorizes a fund in the US Treasury (HRSA’s Countermeasure Injury Compensation Fund) to compensate eligible individuals for serious physical injury or death directly caused by use of MCM covered under declaration
MCM-Related Counterterrorism Legislation

  - Current declarations:
    - Ebola virus disease therapeutics (2/27/2016)
    - Ebola virus disease vaccines (12/3/2015)
    - Pandemic influenza MCMs (1/1/2016)
    - Anthrax MCMs (1/1/2016)
    - Acute radiation syndrome MCMs (1/1/2016)
    - Botulinum toxin MCMs (1/1/2016)
    - Smallpox MCMs (1/1/2016)
MCM-Related Counterterrorism Legislation

- **Pandemic and All Hazards Preparedness Act (PAHPA) (2006)**
  - Established ASPR within HHS
  - Established BARDA
  - Clarified/expanded authorities from 2004 BioShield Act
  - Provided new authorities related to PREP Act
MCM-Related Counterterrorism Legislation

- Pandemic and All Hazards Preparedness Reauthorization Act (PAHPRA) (2013)
  - Reauthorizes provisions of PAHPA
  - Including Special Reserve Fund for MCM
  - Amends FDA’s EUA authority
MCM-Related Counterterrorism Legislation

- Pandemic and All Hazards Preparedness Reauthorization Act (PAHPRA) (2013), con’t.
  - Refinements to existing EUA authorities
    - Provides clearer authority for FDA to issue EUAs BEFORE a CBRN emergency
      - Better enable stakeholders to prepare for use of unapproved MCMs or unapproved uses of approved products
    - Allows the HHS Secretary’s EUA declaration to be based on an HHS determination that there is a significant POTENTIAL for a public health emergency involving a CBRN threat agent, in addition to 3 other types of determinations
Example of EUA Sequence
(note: every situation/MCM is unique, so the sequence could vary)

- *****EVENT*****
- Determination & Declaration
- EUA Request & Authorization
- Countermeasure Distribution
- EUA Conditions
- EUA Termination
Determination & Declaration

- DOD SECRETARY: Determination of Military Emergency or Significant Potential for Military Emergency
- DHS SECRETARY: Determination of Domestic Emergency or Significant Potential for Domestic Emergency
- HHS SECRETARY: Determination of Public Health Emergency or Significant Potential for Public Health Emergency
- DHS SECRETARY: Identification of Material Threat

HHS SECRETARY: Declaration that Circumstances Exist Justifying the EUA
EUA Sequence

- *****EVENT*****
- Determination & Declaration
- EUA Request & Authorization
- Countermeasure Distribution
- EUA Conditions
- EUA Termination
EUA Request, Review & Authorization

Request:

- Government
  - Federal
  - State/Local

- Private Entities
  - Manufacturers
EUA Request, Review & Authorization (cont’d)

FDA Review:

- Review will occur on a case-by-case basis
- Based on scientific data available at time of consideration
- If feasible, consultation to gather additional information
  - National Institutes of Health (NIH) Director
  - CDC Director
  - Assistant Secretary for Preparedness and Response
EUA Request, Review & Authorization (cont’)

FDA Criteria:

1. Agent referred to in the HHS EUA declaration can cause a serious or life-threatening disease or condition

2. It is reasonable to believe that the product MAY be effective in diagnosis, treatment, prevention (based on totality of available scientific evidence)

3. Known and potential benefits of the product outweigh the known and potential risks

4. No adequate, approved, and available alternative
EUA Issuance

- **DOD Secretary**: Determination of Military Emergency or Significant Potential for Military Emergency

- **DHS Secretary**: Determination of Domestic Emergency or Significant Potential for Domestic Emergency

- **HHS Secretary**: Determination of Public Health Emergency or Significant Potential for Public Health Emergency

- **DHS Secretary**: Identification of Material Threat

**HHS Secretary**: Declaration that Circumstances Exist Justifying the EUA

**FDA Commissioner**: Issuance of EUA (if criteria for issuance met)

**Consultation with ASPR, CDC, NIH**
EUA Sequence

- *****EVENT*****
- Determination & Declaration
- EUA Request & Authorization
- Countermeasure Distribution
- EUA Conditions
- EUA Termination
(True or False) The information for providers has to be handed to providers in a written format?

• True
• False
• Unsure
EUA Conditions

- Information for Health Care Providers/Authorized Dispensers*
- Information for Recipients*
- Adverse Event Reporting/Monitoring*
- Recordkeeping/Access*
- Compliance with Good Manufacturing Practices
- Advertising
- Restricted Distribution
- Data Collection/Analysis

* Likely to be a condition
EUA Sequence

- *****EVENT*****
- Determination & Declaration
- EUA Request & Authorization
- Countermeasure Distribution
- EUA Conditions
- EUA Termination
EUA Termination or Revocation

- Circumstances justifying EUA no longer exist or
- Change in the approval status of the product
- Criteria of issuance are no longer met
- Necessary to protect public health or safety
EUA Summary
EUA Bottom Line

- EUA may be applicable for a number of types of medical products
- HHS Secretary needs to declare that circumstances exist to justify issuance of an EUA
- FDA Commissioner issues the EUA
- EUA does not eliminate the need for IND
MCM-Related Counterterrorism Legislation

- Pandemic and All Hazards Preparedness Reauthorization Act (PAHPRA) (2013), con’t.
  - Refinements to existing EUA authorities, con’t.
    - Expands time period for collection and analysis of information about MCMs safety and effectiveness for reasonable period beyond the effective period of the EUA
MCM-Related Counterterrorism Legislation

- Pandemic and All Hazards Preparedness Reauthorization Act (PAHPRA) (2013), con’t.

  • Governmental Pre-positioning allowed
    - Permits federal, state, and local governments to pre-position MCMs in anticipation of FDA approval or clearance, or issuance of an EUA
      - Better prepare for potential rapid deployment during actual CBRN emergency
MCM-Related Counterterrorism Legislation

- Pandemic and All Hazards Preparedness Reauthorization Act (PAHPRA) (2013), con’t.
  - New Authorities for Emergency Use of Approved MCMs
    - New authorities only apply to approved MCMs
    - Expressly empowers FDA to extend the expiration dating/shelf-life of an eligible FDA-approved MCM stockpiled for use in a CBRN emergency and to require appropriate conditions relating to such extensions (storage, sampling, labeling)
Other Programs Affecting MCM in an Emergency

- **FDA/DoD Shelf-life Extension Program (SLEP)**
  - Established in 1986 under an interagency agreement between DoD and FDA
  - Through the Defense Medical Standardization Board, DoD performs programmatic and administrative functions
    - Identifies FDA products/lots to be tested
    - Updates SLEP expiration date database
    - Informs FDA of products eligible for testing
    - Computes financial benefits and cost; bills participants
Other Programs Affecting MCM in an Emergency

- **FDA/DoD Shelf-life Extension Program (SLEP)**
  - FDA performs testing and evaluation of drugs
    - Determines appropriate tests and methods
    - Tests product samples
    - Analyzes results for determining expiration extension
    - Performs research to address SLEP issues
Other Programs Affecting MCM in an Emergency

- **FDA/DoD Shelf-life Extension Program (SLEP)**
  
  - SLEP is a fee for service program
  
  - Open to Federal Participants who sign memorandum of agreement with FDA
    
    - US Army, Navy, Air Force, Marines
    - Strategic National Stockpile
    - Department of Veterans Affairs
    - US Postal Service
    - Bureau of Federal Prisons
Other Programs Affecting MCM in an Emergency

- FDA/DoD Shelf-life Extension Program (SLEP)
  - Large stockpiles/environmentally controlled
  - Drugs not biologics
  - Limited commercial use, military use, or large quantities
  - Provision for relabeling
    - Capacity exceeded
    - Dear Doctor letters
    - Database maintained
    - Exploring new avenues for the future
  - Products that fail testing are destroyed
MCM-Related Counterterrorism Legislation

- Pandemic and All Hazards Preparedness Reauthorization Act (PAHPRA) (2013), con’t.
  - New Authorities for Emergency Use of MCM, con’t.
    - Allows CDC to create and issue, and government stakeholders to disseminate, emergency use instructions (EUI) (also referred to as fact sheets for recipients and health care professionals), about the FDA approved conditions of use for such MCMs before a CBRN event occurs
Why EUI?
2009 H1N1 Pandemic EUA Experiences

- FDA-approved label = narrow scope

- Event-driven aspects of MCM distribution and usage led to FDA deeming a product use no longer approved:
  - Mass-dispensing at pods and postal delivery of MCMs
  - Without prescribing and dispensing label requirements
  - Partial dispensing of initial start-up doses
  - Dispensed without FDA-required medication guides (if applicable)
  - Shelf-life extension
  - Information sheets specific to the emergency
Regulatory Mechanisms: EUI

- **Objective**: A MORE streamlined process that allows delivery of FDA-approved medical products for treatment/prophylaxis of the affected population in an emergency
  - SLTT implications
    - Quicker implementation and fewer complexities
    - Must still provide instructions to healthcare workers and public

- **What else about EUI?**
  - CDC authority, not FDA (found in the FD&C Act, but delegated to CDC)
    - Instruction/fact sheets provided by CDC for FDA-approved drugs for a specific threat that would otherwise require an EUA
      - Example: shelf-life extensions
  - Charter
    - Reviewing fact sheet clearance process, reviewing information to go on the fact sheets
    - Reviewing SNS MCMs that may be considered for EUI
Regulatory Mechanisms: EUI

- Facilitates MCM use without violating the FD&C Act
- Authorizes issuance of Emergency Use Instructions for FDA-approved MCMs concerning their approved conditions of use in an emergency or potential emergency

- Intended to inform:
  - Healthcare providers during an emergency
  - Recipients to whom the “eligible product” is to be administered.

- Provides information regarding the event and disease or condition
- Liability protection (except for willful misconduct) for MCM use
## EUA vs EUI

<table>
<thead>
<tr>
<th>EUA</th>
<th>EUI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Determination and Declaration</td>
<td>Determination</td>
</tr>
<tr>
<td>Unapproved MCM or unapproved use of an approved MCM (off-label use)</td>
<td>Approved MCM and “approved conditions of use”</td>
</tr>
<tr>
<td>FDA reviews and authorizes</td>
<td>CDC develops and issues</td>
</tr>
<tr>
<td>EUA Conditions</td>
<td>No Conditions</td>
</tr>
<tr>
<td>Eligible for PREP Act coverage</td>
<td>Eligible for PREP Act coverage</td>
</tr>
</tbody>
</table>
## EUA vs EUI

<table>
<thead>
<tr>
<th></th>
<th>Emergency Use Instructions (EUI)</th>
<th>Emergency Use Authorization (EUA)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Fact Sheets</strong></td>
<td>CDC issued, states have option to include state specific contact info</td>
<td>FDA issues template, states can create own version if consistent with FDA version</td>
</tr>
<tr>
<td><strong>Adverse Event Monitoring/Reporting</strong></td>
<td>May be required</td>
<td>Required</td>
</tr>
<tr>
<td><strong>Recordkeeping/Access</strong></td>
<td>Product distribution and patient tracking May be required</td>
<td>Required for manufacturers and possibly others</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>Determination expires or EUI revoked by CDC Director</td>
<td>Circumstances justifying EUA no longer exist or change in product’s approval status</td>
</tr>
</tbody>
</table>
Examples of EUI MCMs

- **EUI-eligible MCMs**
  - Doxycycline/Ciprofloxacin for PEP & treatment of anthrax
  - Tamiflu/Relenza for PEP & treatment of acute, uncomplicated influenza; treatment of complicated, hospitalized influenza

- **Ineligible MCMs**
  - Tecovirimat for smallpox
  - Amoxicillin for anthrax
  - BioThrax for PEP in children

- **Potential EUI-eligible MCMs**
  - Neupogen for H-ARS with modified dosing instructions
  - BioThrax for PEP in adults with modified dose or schedule
  - Radiogardase in age groups not covered in FDA-approved package insert
EUI for PEP of Inhalation Anthrax

- Ciprofloxacin
  - EUI for Healthcare Providers
  - EUI for Recipients

- Doxycycline
  - EUI for Healthcare Providers
  - EUI for Recipients
  - Crushing instructions pamphlet and 1-pager
  - Crushing instructions video
    (https://www.youtube.com/watch?v=Wecask69YXw)
EUI for PEP of Inhalation Anthrax

▪ Before an emergency:
  • Documents posted on password-protected CDC JOIN SharePoint for sharing with external public health partners

▪ During an emergency:
  • Will be posted on CDC’s public website
MCM-Related Counterterrorism Legislation

- Pandemic and All Hazards Preparedness Reauthorization Act (PAHPRA) (2013), con’t.
  - New Authorities for Emergency Use of MCM, con’t.
    - Permits FDA to waive otherwise applicable manufacturing requirements (current Good Manufacturing Practices) such as storage or handling, to accommodate emergency response needs
MCM-Related Counterterrorism Legislation

- Pandemic and All Hazards Preparedness Reauthorization Act (PAHPRA) (2013), con’t.
  - New Authorities for Emergency Use of MCM, con’t.
    - Allows for emergency dispensing (including mass dispensing at a POD) of MCMs during an actual CBRN emergency without requiring an individual prescription for each recipient of the MCM, if (1) permitted by state law or (2) in accordance with an order issued by FDA
Emergency Dispensing Orders

- FDA issued two emergency dispensing orders on April 13, 2016 for ciprofloxacin and doxycycline for anthrax post-exposure prophylaxis

- “Order Permitting Emergency Dispensing of Oral Formulations of Doxycycline and Waiver of cGMP Requirements During an Anthrax Emergency”
  - Without an individual prescription
  - Without all other information otherwise required to be provided with product
  - Not supplied in unit of use container
  - Partial supplies
  - Temperature excursions that do not exceed 40°C < 7 days
MCM-Related Counterterrorism Legislation

- Pandemic and All Hazards Preparedness Reauthorization Act (PAHPRA) (2013), con’t.
  - New Authorities for Emergency Use of MCM, con’t.
    - Expands the current waiver authority for risk evaluation and mitigation strategies (REMS) to encompass ANY element for MCMs to mitigate the health effects of a CBRN emergency.
Drug Supply Chain Security Act

- Title II of the Drug Quality and Security Act of 2013
- Outlines critical steps to build an electronic, interoperable system to identify and trace certain prescription drugs as they are distributed in the U.S.
- Ten years after enactment, the system will facilitate the exchange of information at the individual package level about where a drug has been in the supply chain.
Other MCM-Related Legislation

- **Drug Supply Chain Security Act, con’t.**
  - The new system will:
    - Enable verification of the legitimacy of the drug product identifier down to the package level
    - Enhance detection and notification of illegitimate products in the drug supply chain
    - Facilitate more efficient recalls of drug products
Other MCM-Related Legislation

- Drug Supply Chain Security Act, con’t.
  - Collaborative effort between FDA with drug manufacturers, wholesale drug distributors, repackagers, dispensers (primarily pharmacies), also affects third-party logistics providers
Drug Supply Chain Security Act, con’t.

- Key provisions to be implemented over next 10 years:
  - Product identification
  - Product tracing
  - Product verification
  - Detection and response
  - Notification
  - Wholesaler licensing
  - Third-party logistics provider licensing
Drug Supply Chain Security Act, con’t.

• Various provisions have started
  
  ▶ 2015: Provide product tracing information (manufacturers, repackagers, wholesale distributors, dispensers)
  
  ▶ 2015: Know how to handle suspect and illegitimate product (manufacturers, repackagers, wholesale distributors, dispensers)

  ◆ Establish systems to quarantine and investigate suspect product
  
  ◆ Notify FDA and trading partners if illegitimate product is found
Drug Supply Chain Security Act, con’t.

- Various provisions have started
  - 2015: Confirm authorized trading partners (manufacturers, repackagers, wholesale distributors, dispensers, and third-party logistics providers)
    - Check with state authority or FDA’s drug establishment registration database to confirm authorization or licensure
  - 2014-15: Report licensure (third party logistics providers and wholesale distributors)
    - Report licensure and other information to FDA
Other MCM-Related Legislation

- Drug Supply Chain Security Act, con’t.
  - Various guidances have been issues by FDA
  - Example: “Requirements for Transactions with First Responders under Section 582 of the Federal Food, Drug, and Cosmetic Act – Compliance Policy Guidance for Industry” (February 2016)
    - FDA does not intend to take action against:
      - A dispenser who transfers ownership of a product directly to a first responder without providing tracing information
      - Trading partners who conduct business with a first responder that is not authorized as a dispenser
      - A first responder who accepts ownership of product without receiving tracing information and does not capture and maintain product tracing information, or who does not comply with dispenser requirements for verification of suspect or illegitimate product
Drug Supply Chain Security Act, con’t.

- Some programs have been granted waivers, i.e. Vaccines for Children program
- Others have asked for waivers and are working with FDA to find best path forward:
  - Strategic National Stockpile
  - CDC Drug Service
References

FDA Draft EUA Guidance:
http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm

FDA EUA site:
http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm

Public Readiness and Emergency Preparedness Act (PREP Act):

Emergency Dispensing Orders
http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm495126.htm

PAHPRA summary
http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm411434.htm
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How valuable did you find this webinar?

• Very valuable
• Moderately valuable
• Minimally valuable

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[Open ended question]
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Questions for all speakers
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