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WEBINAR SERIES

Recent Developments in FDA's Emergency Authority for Medical Countermeasures

U.S. Food and Drug Administration, Office of the Commissioner, Office of Counterterrorism and Emerging Threats

American Society of Law, Medicine & Ethics
Public Health Law Association
Network for Public Health Law
Public Health Law Research Program

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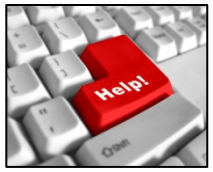

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- A series focused on providing substantive knowledge on important issues in public health law
  - May qualify for CLE credits, details will be sent after the webinar
- Geared toward anyone committed to public health
  - Including public health lawyers, officials, practitioners, policy-makers, advocates, and more
- Webinar series partners include:
  - American Society of Law, Medicine & Ethics
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- Next webinar is Thursday, April 19th 1-2 p.m. EDT

  Nutrition As A Winnable Battle

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Overview of Presentations

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The legal information and assistance provided in this webinar does not constitute legal advice or legal representation, nor reflect the opinion of the series partners.

Overview

- FDA's Roles in Regulating Medical Products and Medical Countermeasures (MCMs)
- Legal and Regulatory Mechanisms for the Use of MCMs
  - Investigational New Drug Application (IND)
  - Emergency Use Authorization (EUA)
- Recent Issues and Developments Related to State and Local Mass Dispensing Efforts

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FDA's Roles in Regulating Medical Products and Medical Countermeasures (MCMs)

Heather McDowell, JD

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Overview of FDA's Roles

- An agency within HHS, FDA is responsible for:
  - Protecting public health by assuring foods are safe, wholesome, sanitary, and properly labeled, and human and veterinary drugs, vaccines, other biological products, and medical devices intended for human use are safe and effective
  - Protecting public from electronic product radiation
  - Assuring cosmetics and dietary supplements are safe/properly labeled
  - Regulating tobacco products
  - Advancing public health by helping to speed product innovations
  - Helping public get accurate science-based information they need to use medicines, devices, and foods to improve their health
- Geographic scope
  - 50 States, District of Columbia, Puerto Rico, Guam, Virgin Islands, American Samoa, and other U.S. territories and possessions

Brief History of FDA Regulation

- **Food and Drugs Act (1906):** 1st comprehensive federal consumer protection law; prohibited misbranded and adulterated food and drugs in interstate commerce

- **Food, Drug, and Cosmetic Act (1938):** Tightened controls over drugs, as well as food, cosmetics, & medical devices; first time firms must show drugs are safe and include adequate directions for safe use; biologics treated as drugs
  - Still in force today (as amended); some notable milestones include:
    - *Kefauver-Harris Drug Amendments (1962)* - required firms to prove effectiveness of drugs before marketing
    - *Medical Device Amendments (1976)* - applied safety and effectiveness safeguards to new devices
    - *Project BioShield Act of 2004* - allows FDA to authorize emergency use of unapproved products, and unapproved uses of approved products

- **Today:** FDA, as part of its public health mission, monitors the manufacture, import, transport, storage, and sale of $1 trillion worth of goods annually

FDA Regulation of Medical Products

- Among the products FDA regulates are 3 categories of diagnostic, preventive, or therapeutic products:
  - **Drugs** (e.g., antibiotics)
    - Center for Drug Evaluation and Research (CDER)
  - **Biologics** (e.g., vaccines)
    - Center for Biologics Evaluation and Research (CBER)
  - **Medical devices** [e.g., in vitro diagnostics (IVDs); ventilators]
    - Center for Devices and Radiological Health (CDRH)
- Legal and regulatory authorities
  - Federal Food, Drug, and Cosmetic (FD&C) Act (as amended)
    - 21 U.S.C. 301 *et seq.;* 21 C.F.R. (Food and Drugs)
  - Public Health Service (PHS) Act (as amended)
    - 42 U.S.C. 262, 264, 266, 282; 21 C.F.R. 601.2(a)

Review and Approval—The Basics

- Sponsor submits data to FDA to seek permission to market its product with specific labeling for a specific purpose
  - **Drugs:** New Drug Application (NDA), Abbreviated NDA (ANDA), Supplemental NDA (sNDA)
  - **Biologics:** Biologics License Application (BLA)
  - **Devices:** Premarket Approval (PMA), 510(k) Premarket Notification
- Risk-benefit analysis
- Labeling
- Expiry dating
- Current Good Manufacturing Practices (CGMPs)

Enforcement

- FDA enforces the FD&C Act and certain related statutes
  - e.g.) provisions of the PHS Act relating to the approval of biological products
- FDA also enforces its regulations, which are based on those statutes
- In some cases, as with all law enforcement agencies, FDA recognizes that there are technical violations of its statutes and regulations for which enforcement is inappropriate
  - In such cases, FDA can exercise its enforcement discretion

Practice of Medicine

- FDA generally does not regulate the practice of medicine
  - Once a product is approved or cleared, a licensed health care professional has the freedom to use that product for any purpose, even if the use is inconsistent with the product's approved labeling
  - Even in the midst of a public health emergency, FDA does not regulate the practice of medicine
- However, to protect the public's health, FDA and the courts are very strict in preventing marketers from promoting products for uses for which they are not approved or cleared by FDA

How Does This All Apply to MCMs?

- MCMs defined
  - The drugs, vaccines, and medical devices used to mitigate or prevent the human health effects of chemical, biological, radiological, or nuclear (CBRN) emergencies (e.g., an anthrax attack or influenza pandemic)
- Some MCMs are intended to be used during emergencies consistent with their approved labeling
  - No need for further FDA review/authorization
- Other MCMs are intended to be used during emergencies in ways beyond their FDA-approved labeling (e.g., without a prescription; different dosing)
  - Special legal/regulatory approaches needed
- Other MCMs are not yet FDA-approved for *any* use, but might be helpful for an emergency response because of the lack of other suitable alternatives
  - Special legal/regulatory approaches needed

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Legal and Regulatory Mechanisms for the Use of MCMs

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Office of Counterterrorism and Emerging Threats (OCET)

- Coordinates portfolio of FDA counterterrorism and pandemic influenza policy and planning initiatives

- Develops and coordinates implementation of FDA policies to ensure safe and effective MCMs (drugs, biologics, & medical devices) are available to counter CBRN agents

- Collaborates closely with FDA Centers/Offices and external partners to develop and coordinate implementation of preparedness plans and programs to counter emerging threats

- Leads FDA's EUA activities

- Coordinates the Medical Countermeasures Initiative (MCMi)

Medical Countermeasures Initiative (MCMi)

- Launched in August 2010 to build upon the ongoing work at FDA to ensure the nation has the necessary MCMs for high-priority CBRN and emerging infectious disease threats

- **Mission:** To promote the development of MCMs by enhancing FDA's regulatory processes and fostering establishment of clear regulatory pathways for MCMs; to facilitate timely access to MCMs by establishing effective regulatory policies and mechanisms

- 3-Pillar approach:
  - I – Enhancing regulatory review processes for the highest priority MCMs and related technologies
  - II – Advancing regulatory science for MCM development and evaluation
  - **III – Modernizing the legal, regulatory, and policy framework for effective public health response**

Investigational New Drug Applications (INDs)

- To be used in human testing in the U.S., in most cases:
  - A drug, including a biologic drug, must be covered by an IND
  - A device must be covered by an investigational device exemption (IDE)
- INDs and IDEs are reviewed by FDA, which has the authority to halt investigations proposed to be carried out under these applications
- IND and IDE regulations require patient safeguards, including in most cases:
  - Institutional Review Board (IRB) supervision
  - Informed consent by subjects
  - Reporting to FDA

Investigational New Drug Applications (INDs)

- In some circumstances, the IND authority may be an appropriate mechanism for use of an unapproved product during a public health emergency

- Types of INDs:
  - *Emergency use IND*
    - Individual/single patient access for serious diseases
  - *Expanded access trial under an IND*
    - Intermediate-sized patient populations
  - *Treatment use IND*
    - Widespread access

Emergency Use Authorizations (EUAs)

- Section 564 of the FD&C Act; established by Project BioShield Act (2004)

- In certain emergency circumstances, FDA's EUA authority may be an appropriate mechanism to authorize the:
  - (1) Use of a product (drug, biologic, or device) that is NOT yet FDA-approved or
  - (2) Unapproved use of an FDA-approved product

- Typically, FDA receives requests for EUAs from federal partners (e.g., CDC) or from product manufacturers

- Use under an EUA is not investigational, so IRB approval and informed consent are not required; alternative dispensing mechanisms can be authorized

- Published in *Federal Register* and posted on FDA website after issuance

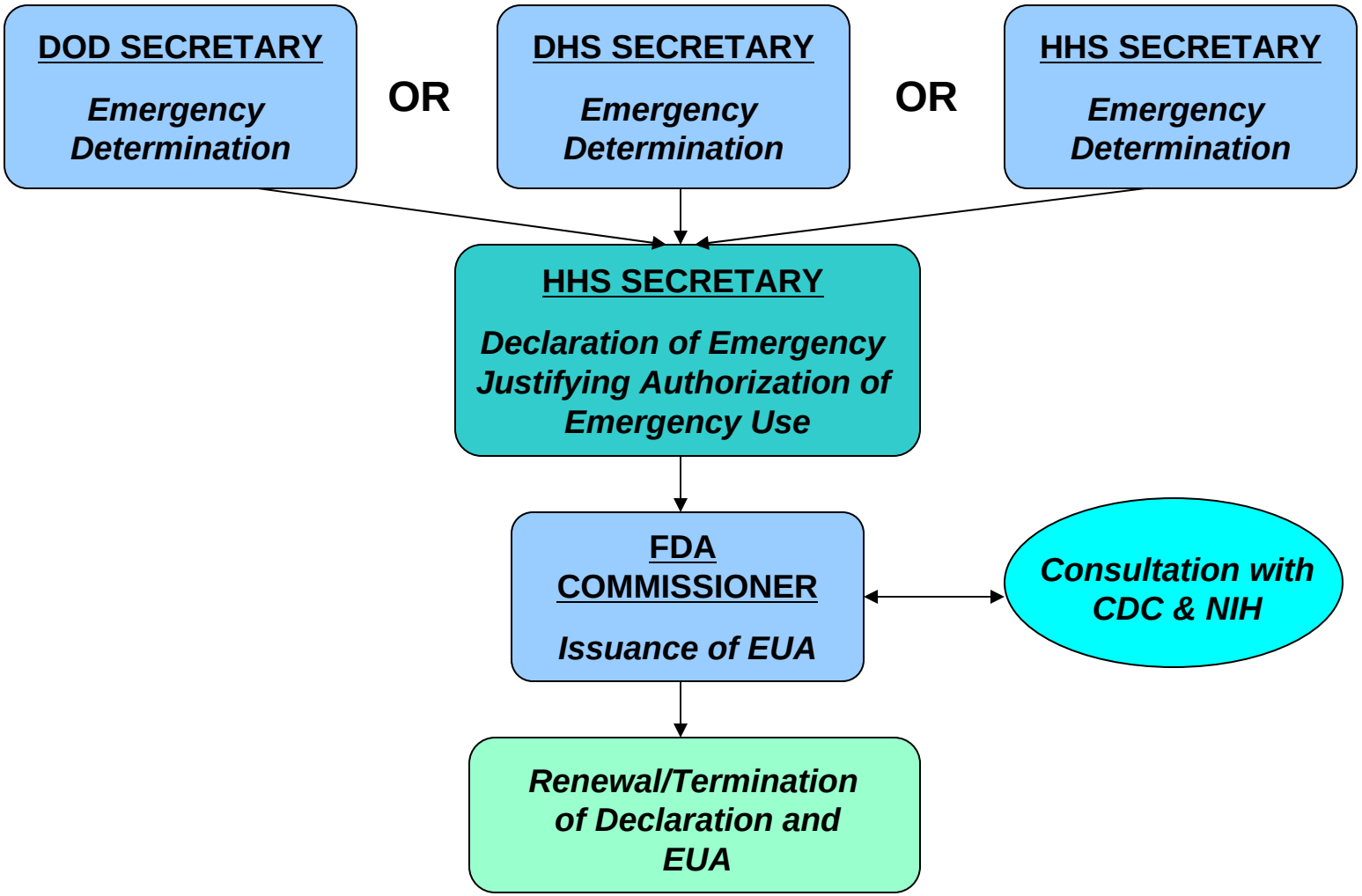
Emergency Use Authorizations (EUAs)

- Why would an EUA be needed?
  - Novel/investigational products may be the best available products to meet the needs of a particular emergency
  - Requirements for clinical investigations or expanded access would be difficult to meet in emergency mass dispensing or mass vaccination scenarios
  - Changes from FDA-approved labeling, expiration dating, dosing schedules, and prescribing requirements would render the product misbranded or unapproved under FDA law
  - Potential gap exists for Public Readiness and Emergency Preparedness (PREP) Act liability coverage
    - PREP Act declarations can cover MCMs that are authorized for use under EUAs

Emergency Use Authorizations (EUAs)

- If FDA grants an EUA request, it is finding that—during a particular type of emergency—if the EUA's conditions are observed:
  - An FDA-approved product may be used in a way inconsistent with the limitations of its approval, or
  - A product that is not yet approved by FDA may be permitted to be used
- Criteria for issuing an EUA
  - Serious or life-threatening illness/condition caused by CBRN agent
  - Reasonable belief product may be effective
  - Known/potential benefits outweigh known/potential risks
  - No adequate, approved, available alternative to product
- Conditions of authorization address required elements of the EUA, such as:
  - Information to be provided on the emergency use (e.g., fact sheets for recipients)
  - Dispensing/screening procedures
  - Monitoring of adverse events; waiver of CGMP requirements; etc.

Steps for Issuing an EUA



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Recent Issues and Developments Related to State and Local Mass Dispensing Efforts

Brooke Courtney, JD, MPH

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Emergency Use Authorizations (EUAs)

- Pre-EUA activity (*ongoing*)

- EUAs issued to date:
  - Department of Defense (anthrax vaccine) (2005) (*terminated*)
  - H1N1 Influenza Pandemic (2009) (*terminated*)
    - Drugs (antivirals—multiple EUAs)
    - Devices (IVDs—multiple EUAs)
    - Personal protective equipment (PPE)
  - Mass Dispensing (doxycycline) (2011) (*current*)
  - National Postal Model (doxycycline home and workplace kits for eligible USPS employee volunteers and family members) (2011) (*current*)

Recent EUA Activity: Doxycycline Mass Dispensing EUA

- Requested by CDC; issued July 21, 2011
- Covers oral formulations of doxycycline products (capsule, tablet, & liquid formulations) for post-exposure prophylaxis (PEP) of inhalational anthrax
- Goal was to facilitate local, state, and federal stakeholders' preparedness and response activities that might otherwise violate provisions of the FD&C Act, such as the:
  - Dispensing of doxycycline without a prescription
  - "Minimum elements" of information to provide flexibility in developing fact sheets for health care professionals and recipients
  - Pre-event storage or distribution of doxycycline packaged or repackaged for emergency distribution
  - Dispensing of a partial supply (e.g., 10 days) of full 60-day regimen

Recent EUA Activity: Doxycycline Mass Dispensing EUA

- This EUA could be issued because of:
  - DHS Secretary's determination of significant potential for a domestic emergency involving *B. anthracis* (2008)
  - HHS Secretary's declaration of emergency justifying the authorization of emergency use of doxycycline hyclate tablets for PEP (2008, 2009, 2010)
  - HHS Secretary's renewal and amendment of the above HHS declaration to apply to all oral formulations of doxycycline (July 20, 2011)

- Additional information:
  - Letter of authorization (76 Fed. Reg. 47197)
    - http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/UCM264104.pdf
  - HHS declaration justifying authorization of emergency use (76 Fed. Reg. 44926)
    - http://www.gpo.gov/fdsys/pkg/FR-2011-07-27/pdf/2011-18937.pdf
  - Questions and answers
    - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm269226.htm

Recent EUA Activity: National Postal Model (NPM) EUA

- In 2008, FDA issued an EUA for doxycycline hyclate tablets contained in individual workplace and household emergency antibiotic kits ("HAKs") for eligible USPS employee volunteers in the Cities Readiness Initiative (CRI) and their household members (*amended and reissued in 2009 & 2010*)

- In 2011, additional amendments were requested by ASPR/BARDA to reflect programmatic changes (e.g., updated fact sheets, screening forms, program name)

- Issued on October 14, 2011

- Covers doxycycline hyclate tablet emergency kits ("HAKs") for PEP of inhalational anthrax; limited to eligible USPS employee volunteers in the NPM and their household members

- Letter of authorization (76 Fed. Reg. 72935)
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm

Other Updates and Developments

- Expiry dating
  - Antiviral drugs in state and local stockpiles
  - Shelf-Life Extension Program (SLEP)
  - Relabeling options (www.fda.gov/edrls)
- MedKits
- Ciprofloxacin
- Reauthorization of Pandemic and All-Hazards Preparedness Act (PAHPA)
  - S. 1855
  - H.R. 2405

Additional Resources

- FDA state & local stakeholder site
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm234336.htm
- EUA questions & answers
  - http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm153297.htm
- EUA guidance
  - http://www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm
- Current & expired/terminated EUAs
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm
- FDA Medical Countermeasures Initiative (MCMi)
  - www.fda.gov/medicalcountermeasures
- PREP Act
  - http://www.phe.gov/Preparedness/legal/prepact/Pages/default.aspx

Additional Resources

- Food and Drug Law Institute. Food and Drug Law and Regulation (2d ed.), *Medical Countermeasures: Emergency Preparedness and Response Roles and Authorities* (Courtney B, Sadove E). 2012.

- Institute of Medicine. *Prepositioning Antibiotics for Anthrax*. 2011.

- Institute of Medicine. *Medical Countermeasures Dispensing: Emergency Use Authorization and the Postal Model: Workshop Summary*. 2010.

- Sherman SE, Foster J, Vaid S. Emergency use authority and 2009 H1N1 influenza. *Biosecur Bioterror* 2009;7(3):245-250.

- Quinn SC, et al. Public willingness to take a vaccine or drug under emergency use authorization during the 2009 H1N1 pandemic. *Biosecur Bioterror* 2009;7(3):275-290.

- Birnkrant D, Cox E. The emergency use authorization of peramivir for treatment of 2009 H1N1 influenza. *NEJM* 2009; 361(23):2204-2207.

THANK YOU!

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Question & Answer

Type your question in through the Q and A panel