FEDERAL UPDATES ON THE EMERGENCY USE OF MCMs: EUAs, EUIs, AND BEYOND

2015 Public Health Preparedness Summit

Atlanta, GA

April 14, 2015

1:30-3:00 pm

U.S. Food and Drug Administration
Medical Countermeasures Initiative

OVERVIEW

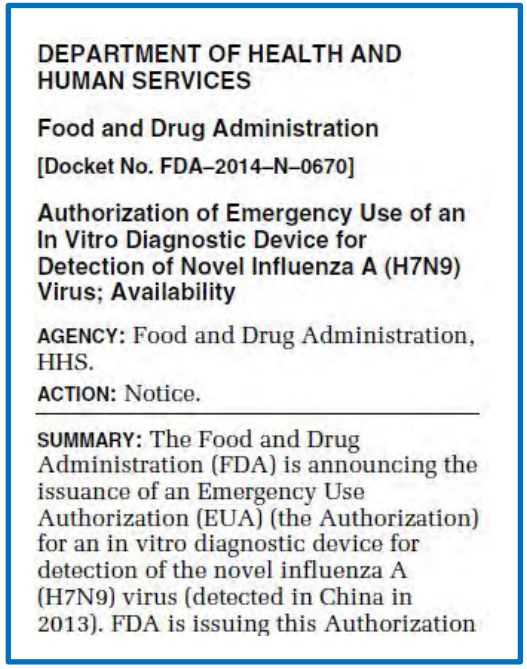
- Recap since last year's Summit (Brooke Courtney)
- FDA: Emergency use authorities and updates (Liz Sadove)
- CDC: PAHPRA – EUI and PREP Act (Joe Foster)
  This copy only includes FDA slides
- CDC: EUI updates (Yon Yu)
  This copy only includes FDA slides
- Q&A

So, what have we all been doing?!

Implementing PAHPRA emergency use authorities and enabling access to MCMs that are not yet approved for use

- CDC and FDA have continued to interpret and implement PAHPRA emergency use authorities and flexibilities

- Multiple EUAs have been issued for preparedness and response purposes
  - 2 H7N9 IVD EUAs for preparedness
  - Reissuance of MERS-CoV IVD EUA for preparedness, and…
  - Ebola…



DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. FDA–2014–N–0670]

Authorization of Emergency Use of an In Vitro Diagnostic Device for Detection of Novel Influenza A (H7N9) Virus; Availability

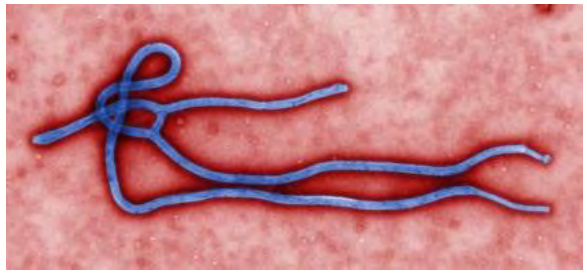
AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the issuance of an Emergency Use Authorization (EUA) (the Authorization) for an in vitro diagnostic device for detection of the novel influenza A (H7N9) virus (detected in China in 2013). FDA is issuing this Authorization

Responding to Emerging Threats: Ebola

- Extensive collaboration/coordination with multiple partners
- EUA declaration issued for Ebola IVDs → 9 EUAs issued for Ebola IVDs (+ many reissued per sponsors' requests)
- PREP Act declaration issued for certain EVD vaccines
- Facilitating export of products
- Facilitating access to investigational products and the development of vaccines and therapeutics (clinical trials, etc.)
- Enforcement of fraudulent product claims
- On-the-ground response
- Etc.



Reviewing and Approving MCM Applications

- Neupogen
  - New indication to increase survival in patients acutely exposed to myelosuppressive doses of radiation (hematopoietic syndrome of ARS)
- Anthrasil, Anthrax Immune Globulin Intravenous
  - To treat patients with inhalational anthrax in combination with appropriate antibacterial drugs
- Influenza A (H5N1) Virus Monovalent Vaccine, Adjuvanted (Q-Pan H5N1)
  - For use in people ≥18 years of age who are at increased risk of exposure to the H5N1 influenza virus
  - 1st adjuvanted vaccine approved for prevention of H5N1 influenza
- Diagnostics
  - e.g.) CDC assay for qualitative detection of plasmid and chromosomal DNA sequences from *B. anthracis* (anthrax)
  - e.g.) 2 IVDs for qualitative detection and differentiation of influenza viruses and modifications of previously approved assays to improve performance

Helping to ensure an adequate supply of MCMs

- Expiry dating extensions
  - Federal Shelf-Life Extension Program (SLEP)
  - Auto-injectors for chemical nerve agents
    - Multiple extensions (most recently March 27, 2015)
    - "DuoDote, AtroPen, CANA, Morphine Sulfate, and Pralidoxime Chloride auto-injectors manufactured by Meridian Medical Technologies nearing or beyond their labeled or extended expiration dates should be retained until further guidance is provided by FDA"
- Exploring possible shelf life/stockpiling solutions for state and local stakeholders
  - e.g) feasibility of using 3rd party testers/laboratories for stability testing (2007 KI guidance)??

Additional Resources

- **PAHPRA (Public Law 113-5)**
  - http://www.gpo.gov/fdsys/pkg/PLAW-113publ5/pdf/PLAW-113publ5.pdf
- **FDA EUA Website** (*official updates, current & terminated EUAs, questions & answers, guidance, etc*.)
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm
- **FDA PAHPRA Website** (*PAHPRA summary, official updates, etc.*)
  - http://www.fda.gov/EmergencyPreparedness/MedicalCountermeasures/ucm359581.htm
- **FDA PAHPRA Questions & Answers** (January 2014)
  - http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/UCM380269.pdf
- **FDA Medical Countermeasures Initiative (MCMi)**
  - http://www.fda.gov/medicalcountermeasures
- **DuoDote/Auto-Injector Expiry Dating Extensions**
  - http://www.fda.gov/Drugs/DrugSafety/ucm376367.htm

THANK YOU!

Brooke Courtney, JD, MPH
Sr. Regulatory Counsel
Office of Counterterrorism and Emerging Threats
Office of the Commissioner
U.S. Food and Drug Administration
301.796.0376 (office) / brooke.courtney@fda.hhs.gov

www.fda.gov/medicalcountermeasures / Twitter: @FDA_MCMi

SESSION: FEDERAL UPDATES ON THE EMERGENCY USE OF MCMs: EUAs, EUIs, AND BEYOND

FDA Emergency Use Authorities and Updates

2015 Public Health Preparedness Summit

Atlanta, GA

April 14, 2015

Elizabeth Sadove, JD
Director, MCM Regulatory Policy
Office of Counterterrorism and Emerging Threats
Office of the Commissioner
U.S. Food and Drug Administration

U.S. Food and Drug Administration
Medical Countermeasures Initiative

OVERVIEW

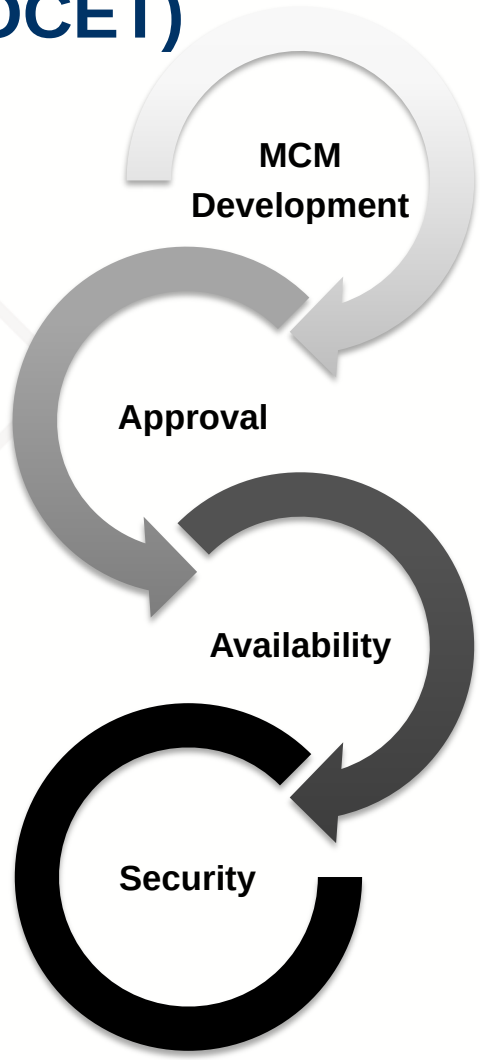
- FDA's MCM Roles
- Ebola Response
- Need for Special Legal/Regulatory Mechanisms for the Emergency Use of MCMs
- Emergency Use Authorization (EUA) & Other Emergency Use Authorities
- Additional Resources

FDA and Counterterrorism

- Protecting the U.S. from threats
  - Chemical, biological, radiological, nuclear (CBRN)
  - Emerging infectious diseases
- Ensuring that medical countermeasures (MCMs) to counter these threats are safe, effective, and secure
  - Drugs, vaccines, diagnostic tests, personal protective equipment (PPE)

Office of Counterterrorism and Emerging Threats (OCET)

- Facilitate the **development** and **availability** of safe, effective MCMs
  - Engage with product sponsors throughout product development
  - Use legal/regulatory mechanisms to facilitate emergency use
  - Monitor for adverse events and assess benefit
  - Ensure laws and policies support this goal
- Point of entry on policy, planning for global health security, counterterrorism, emerging threats
- Identify and resolve complex scientific and regulatory challenges for MCMs



Ebola Response

- Frequent communication and collaboration
  - Internal (FDA agency-wide)
  - HHS partners (BARDA, CDC, NIH/NIAID) and DoD
  - International (e.g., World Health Organization)
- No vaccines or treatments proven to be safe and effective; investigational products in early stages of development
- Facilitate development
  - Active communication with 20+ sponsors
  - Clarify regulatory requirements and expedite review of data
  - Employ drug development programs to expedite development, review and approval (e.g., orphan designation, fast track review, accelerated approval pathway, priority review vouchers)
  - Provide input on preclinical and clinical trial designs (most efficient way to learn if candidate product helps or harms patients)

Ebola Response … continued

- Facilitate access to investigational drugs and devices:
  - IND clinical trials- ethical and fair means to access given limited supplies and need to assess products
  - Expanded access INDs/IDEs
    - Multiple e-INDs issued for patients, not only in U.S. facilities
    - IND protocols for larger populations- if after trial completion and data are promising, FDA could provide wider access
  - Emergency Use Authorization (EUA)
    - Issued multiple EUAs for diagnostics (9 issued, + 6 amended & reissued)
- Export of unapproved products- regulatory considerations
- Consumer protection against fraudulent products/claims
  - 6 Warning Letters as of March 18, 2015
- Liability concerns

Why are legal/regulatory mechanisms for emergency use of MCMs needed?

Without these mechanisms, certain preparedness and response activities could otherwise violate provisions of the FD&C Act:

- Some MCMs needed for a response might not be approved, licensed, or cleared by FDA (e.g., Ebola)
- Some MCMs needed for a response might be approved by FDA, but not for the emergency use (e.g., for a new indication)
- Some might be approved for the emergency use, but:
  - Need to be dispensed (e.g., at PODs) without individual prescriptions and/or by someone who is not a licensed health care professional, and with emergency use instructions (e.g., fact sheets)
  - MCMs might be used beyond their manufacturer-labeled expiration date
- Also, to ensure the Public Readiness and Emergency Preparedness (PREP) Act protections apply

What are the legal/regulatory mechanisms for emergency use of MCMs?

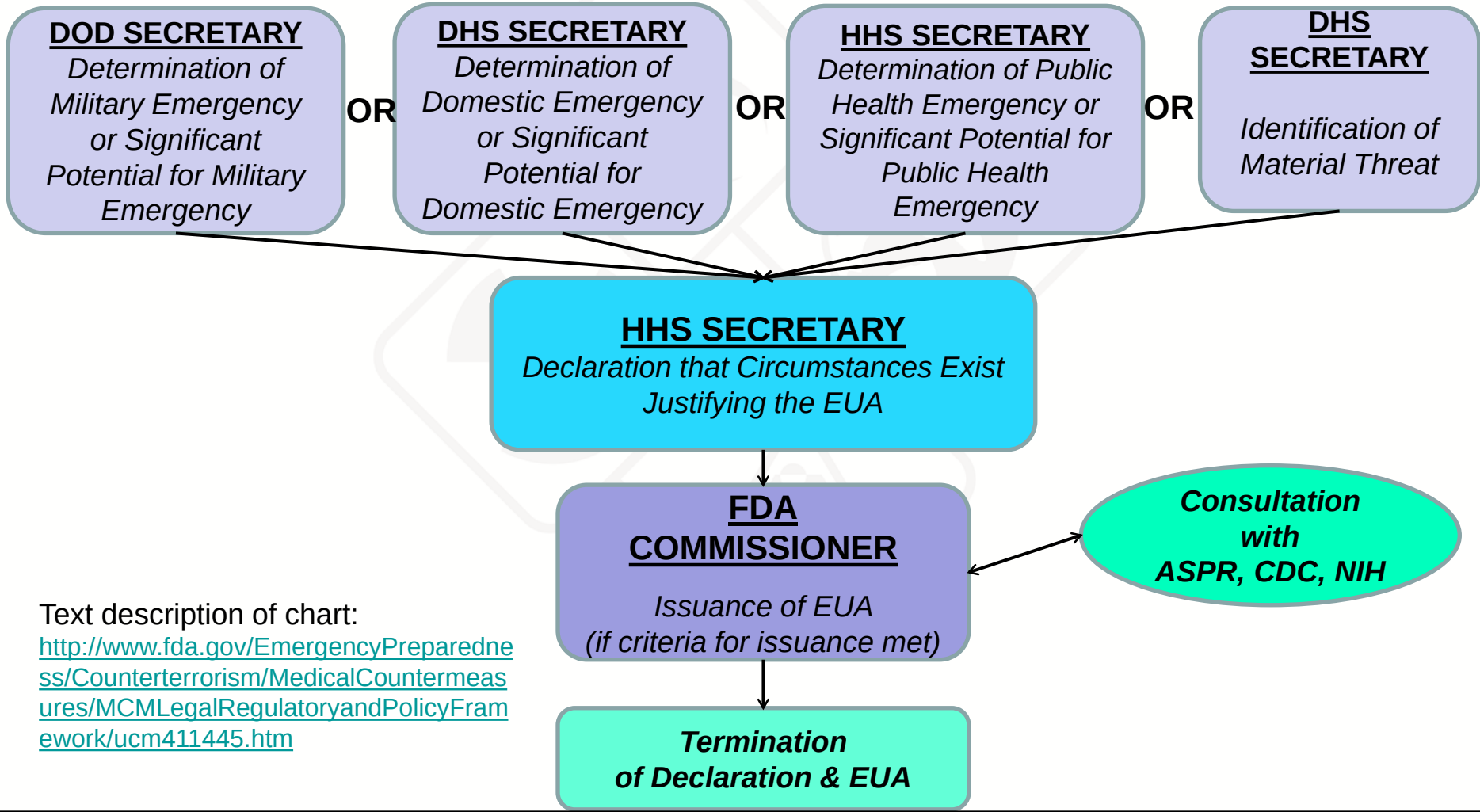
- **Emergency Use Authorization (EUA)**
  - FD&C Act § 564
  - Established by Project BioShield Act (2004)
  - Amended by the Pandemic and All-Hazards Preparedness Reauthorization Act of 2013 (PAHPRA) (Public Law 113-5)
- **Emergency use authorities**
  - FD&C Act §§ 564A, 505-1, and 564B
  - Established by PAHPRA
- **Expanded access to investigational drugs and devices**
  - Investigational New Drug Application (IND) (21 CFR Parts 312.300-320)
  - Investigational Device Exemption (IDE) (21 CFR Part 812)

EUA Authority (FD&C Act § 564)

- With an EUA, FDA can authorize for use in CBRN emergencies the:
  - Use of unapproved MCMs or
  - Unapproved use of approved MCMs (e.g., for a new indication)
- When scientific evidence is available to support MCM use in a CBRN emergency, issuing an EUA enables response stakeholders to use, or prepare to use, an MCM without violating the FD&C Act; also helps to ensure applicable PREP Act coverage
- Overview of requirements for EUA issuance:

1. DHS, DoD, or HHS Secretary makes a specific type of **determination**
2. HHS Secretary issues a **declaration** that circumstances exist to justify EUA issuance based on 1 of the 4 types of determinations ***(this is not a Public Health Emergency declaration; it is specific and unique to EUAs)***
3. FDA ensures EUA **criteria for issuance** are met and issues the EUA when appropriate

Summary of Process for EUA Issuance
(FD&C Act § 564, as amended by PAHPRA)



Text description of chart:
http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm411445.htm

EUA Authority:
PAHPRA Amendments

- Gives FDA clearer authority to issue EUAs before an emergency
  - Allows issuance of an EUA without declaring that an "emergency" exists (e.g., the EUA determination can be based on a "significant potential" for a public health emergency or on the identification of a material threat)
  - To allow for staging (moving product in interstate commerce), stockpiling, creating fact sheets, and rapid initial use
  - Criteria for issuance are the same whether the EUA is issued before or during an emergency
- Eliminates 1-year automatic expiration of the HHS declaration that supports EUA issuance
- Expands the time period for collection and analysis of data about an MCM's safety and clinical benefit beyond the effective period of the EUA
- Expressly permits FDA, when issuing an EUA for use of a diagnostic test, to categorize the test to allow it to be used at a point-of-care site (i.e., for purposes of CLIA waiver)

Example of EUA Process/Issuance

- **Issuance of Department of Defense (DoD) Ebola IVD EUA (8/5/14)**
  - September 22, 2006: DHS Secretary **determined** the Ebola virus presents a material threat against the U.S. population sufficient to affect national security
  - August 5, 2014: HHS Secretary **declared** "*that circumstances exist justifying the authorization of emergency use of in vitro diagnostics for detection of Ebola virus*" (79 FR 47141)
  - August 5, 2014: Based upon a request from DOD, FDA **issued** an EUA for an EUA for the Ebola Zaire (Target 1) (EZ1) Real-Time PCR Assay (79 FR 55804)
  - October 10, 2014: Per DoD request to amend the EUA, FDA **amended and reissued** the EUA in its entirety (no FR notice required)
  - Additional Ebola EUA information is available at: http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm

Summary of EUAs Issued (1)

Year	MCM	Requester	Status
	Anthrax [*Bacillus anthracis*]		
2005	Anthrax Vaccine Adsorbed (AVA)	DoD	Terminated
2008	Doxycycline hyclate tablets (in USPS home & workplace kits)	HHS (ASPR/ BARDA)	Amended in 2009, 2010, 2011 (see row below)
2011	Doxycycline hyclate 100 mg oral tablets (in National Postal Model home 7 workplace kits)	HHS (ASPR/ BARDA)	Current
2011	All oral formulations of doxycycline (mass dispensing)	HHS (CDC)	Current*
	2009 H1N1 Influenza Pandemic		
2009-2010	Antivirals (3)	HHS (CDC)	Terminated
2009-2010	IVDs (18)	Various	Terminated
2009-2010	Disposable N95 Respirators	HHS (CDC)	Terminated

*To be terminated after issuance of doxycycline emergency dispensing order, CGMP waiver, and CDC EUI (sec. 564A of the FD&C Act).

Summary of EUAs Issued (2)

Year	MCM	Requester	Status
	Novel Influenza A (H7N9) Virus		
2013	CDC Human Influenza Virus Real-Time RT-PCR Diagnostic Panel-Influenza A/H7 (Eurasian Lineage) Assay	HHS (CDC)	Current
2014	Lyra™ Influenza A Subtype H7N9 Assay	Quidel Corporation	Current
2014	A/H7N9 Influenza Rapid Test	Arbor Vita Corporation	Current
	Middle East Respiratory Syndrome Coronavirus [MERS-CoV]		
2013	CDC Novel Coronavirus 2012 Real-time RT-PCR Assay	HHS (CDC)	Current

Summary of EUAs Issued (3)

Year	MCM	Requester	Status
	Ebola Virus		
2014 (reissued in 2014)	DoD EZ1 Real-time RT-PCR Assay	DoD	Current
2014 (reissued in 2015)	CDC Ebola VP40 rRT-PCR Assay	CDC	Current
2014 (reissued in 2015)	CDC Ebola NP rRT-PCR Assay	CDC	Current
2014 (reissued in 2015)	BioFire Defense FilmArray NGDS BT-E Assay	BioFire Defense	Current
2014	BioFire Defense FilmArray Biothreat-E test	BioFire Defense	Current
2014 (reissued in 2014)	RealStar® Ebolavirus RT-PCR Kit 1.0	altona Diagnostics GmbH	Current
2014	LightMix® Ebola Zaire rRT-PCR Test	Roche Molecular Systems, Inc.	Current
2015 (reissued in 2015)	ReEBOV™ Antigen Rapid Test	Corgenix	Current
2015	Xpert® Ebola Assay	Cepheid	Current

Other Emergency Use Authorities

- In addition to amending the EUA authority, PAHPRA establishes emergency use authorities for **approved MCMs** to facilitate stakeholder preparedness and response without EUA issuance:
  - Emergency dispensing orders (FDA)
  - Emergency use instructions (EUI) (CDC)
  - Expiration dating extensions (FDA)
  - Current Good Manufacturing Practices (CGMP) waivers (FDA)
  - Risk Evaluation and Mitigation Strategy (REMS) waivers (FDA)
- **Pre-positioning (approved/unapproved MCMs) (FD&C Act §564B):**
  - To facilitate rapid deployment during an actual emergency and without EUA issuance, PAHPRA allows pre-positioning of MCMs by or on behalf of government entities (federal, state, local) in anticipation of FDA approval, clearance, or licensure or EUA issuance
- These authorities preserve otherwise applicable liability protections (e.g., PREP Act) for responders and others involved in MCM planning, preparedness, and response

Emergency Use Authorities

For **FDA-approved MCMs** intended for use during CBRN emergencies, certain activities are allowed ***without FDA issuing an EUA*** and without rendering a product unapproved, adulterated, or misbranded, as follows:

- **Emergency dispensing orders** [§564A(d)]
  - Allows emergency dispensing (e.g., mass dispensing at PODs) of approved MCMs without an individual prescription or without all required labeling information or by non-health care professionals if permitted:
    - (a) under State law or
    - (b) in accordance with an emergency dispensing order issued by FDA
- **Emergency use instructions (EUI)** [§564A(e)]
  - Permits a designated HHS official/unit (delegated to CDC) to create and issue, and others to disseminate, EUI about the use of an approved MCM before or during a CBRN emergency
- **CGMP waivers** [§564A(c)]
  - Deviations from otherwise applicable cGMP requirements (e.g., temporary storage temperature deviations during a response)

Emergency Use Authorities… continued

- **Expiration dating extensions** [§564A(b)]
  - Expressly authorizes FDA to extend expiration beyond labeled expiration date
  - Extensions must be supported by appropriate scientific data
  - Extensions include requirements and conditions (e.g., identification of specific lots and duration of extension; storage and labeling requirements; etc.)
  - Does not expand federal Shelf-Life Extension Program (SLEP) to non-federal MCM stockpiles or create a new program for state/local stakeholders
- **REMS waivers** [§505-1]
  - Expands FDA's authority to waive REMS to cover any element based on scenarios giving rise to an EUA

Summary of PAHPRA's MCM Emergency Preparedness and Response Provisions

MCM Emergency Preparedness and Response Provisions	MCM Category	FD&C Act Section
Amendments to the EUA Authority	***Unapproved MCMs** ***Unapproved uses of approved MCMs**	**§ 564**
Determinations for EUA issuance		§§ 564(b)(1)(A)-(D)
Duration of HHS EUA declaration		§ 564(b)(2)
EUAs issued for preparedness purposes		§ 564(b)(1)
Data collection time period		§ 564(e)(1)(B)(iii)
Categorization of in vitro diagnostics (IVDs)		§ 564(m)
Emergency Use Authorities (No EUA Needed)	***Approved MCMs only**	**§§ 564A & 505-1**
Emergency use instructions (EUI)	*EUI authority delegated to CDC	§ 564A(e)
Emergency dispensing orders		§ 564A(d)
Expiration dating extensions		§ 564A(b)
CGMP waivers		§ 564A(c)
REMS waivers		§ 505-1
Pre-Positioning Authority	***Approved MCMs** ***Unapproved MCMs**	**§ 564B**

Examples of Implementation

- Doxycycline and ciprofloxacin packages (in progress)
  - Emergency dispensing orders, including specific CGMP waivers, in coordination with CDC's issuance of EUIs, will replace the need for EUAs for mass dispensing of doxycycline and ciprofloxacin
  - Emergency use package = emergency dispensing order + CGMP waiver + EUI
  - After issuance, the 2011 doxycycline mass dispensing EUA will be terminated
- Expiration dating extensions
  - Addressing critical stakeholder needs, enabling multiple extensions (e.g., DuoDote auto-injectors)
  - Exploring potential approaches for using authority for possible state/local MCM stockpile extensions (e.g., feasibility of 3rd party laboratory testing of doxycycline and ciprofloxacin) (in progress, very complex!)
- Revision of the 2007 EUA guidance to reflect PAHPRA updates (in progress)

Additional Resources

- **PAHPRA (Public Law 113-5)**
  - http://www.gpo.gov/fdsys/pkg/PLAW-113publ5/pdf/PLAW-113publ5.pdf
- **FDA EUA Website** (*official updates, current & terminated EUAs, questions & answers, guidance, etc*.)
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm
- **FDA PAHPRA Website** (*PAHPRA summary, official updates, etc.*)
  - http://www.fda.gov/EmergencyPreparedness/MedicalCountermeasures/ucm359581.htm
- **FDA PAHPRA Questions & Answers** (January 2014)
  - http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/UCM380269.pdf
- **FDA Medical Countermeasures Initiative (MCMi)**
  - http://www.fda.gov/medicalcountermeasures
- **PREP Act (HHS)**
  - http://www.phe.gov/Preparedness/legal/prepact/Pages/default.aspx

Please contact FDA with questions about MCM emergency use authorities, expiry dating challenges, etc.

THANK YOU!

www.fda.gov/medicalcountermeasures

Twitter: @**FDA_MCMi**

U.S. Food and Drug Administration
Medical Countermeasures