Emergency Use of Medical Countermeasures: FDA Roles and Authorities

University of Arizona
Regulatory Science Series

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Office of the Commissioner
Examples of Evolving Threat Space

Early 1980’s...

Accumulation of emerging/reemerging infectious diseases

Overview of Public Health Legal Preparedness
Public Health Legal Preparedness

• Term first appeared in late 1990s; subset of public health preparedness

• Recognizes the essential role law plays in protecting the public from catastrophic health events
  ▪ Core foundation to ensure U.S. is prepared to prevent, respond to, and reduce adverse effects of public health emergencies

• May impact a range of players during disasters
  ▪ e.g.) health officials, hospitals, health care practitioners, first responders, businesses, medical countermeasure (MCM) manufacturers, public, etc.

Levels (and Layers) of Authority

- **Global**
  - WHO (Director-General) (e.g., IHR, PHEIC declaration)
  - Individual countries (substantial variation in laws, capabilities, declarations)

- **Federal** (e.g., President, Cabinet Secretaries)
  - e.g.) emergency laws, declarations

- **State** (e.g., Governor, Secretary of Health)
  - e.g.) traditional public health powers (police powers), emergency laws and declarations (much variation)

- **Local** (e.g., Mayor, County Executive, Health Officer)
Examples of Legal Preparedness/Response Tools

- Declarations
- Executive orders
- Isolation and quarantine authorities (federal and state)
- Volunteer and other liability protections
- 1135 waivers
- Mutual aid agreements—Emergency Management Assistance Compact (EMAC)
- Emergency use authorities for MCMs

www.fda.gov
FDA Roles
Counterterrorism and Emerging Threats

• Protecting the U.S. (civilians & the warfighter) from threats
  ▪ Chemical, biological, radiological, and nuclear (CBRN)
  ▪ Emerging infectious diseases
  ▪ Agents of war (warfighter)

• Ensuring medical countermeasures (MCMs) to counter these threats are safe, effective, and secure
  ▪ Drugs, biologics/vaccines, devices

• FDA Office of Counterterrorism and Emerging Threats
  ▪ Coordinates FDA’s Medical Countermeasures Initiative (MCMi) efforts closely with CBER, CDER, CDRH, and other FDA centers and offices
  ▪ Facilitates development and availability of safe, effective MCMs (goal is product approval)
  ▪ Identifies/works to resolve complex scientific and regulatory challenges within FDA and with USG partners (including PHEMCE)
  ▪ Serves as point of entry on policy and planning for global health security, counterterrorism, emerging threats
Public Health Emergency Medical Countermeasures Enterprise (PHEMCE)

Key
- PHEMCE Mission Components
- HHS PHEMCE Agencies
- Non-HHS PHEMCE Agencies
- Non-Federal Stakeholders

Acronyms
- PHEMCE: Public Health Emergency Medical Countermeasures Enterprise
- DHS: Department of Homeland Security
- DoD: Department of Defense
- USDA: U.S. Department of Agriculture
- VA: Department of Veterans Affairs
- HHS: Department of Health and Human Services
- ASPR: Assistant Secretary for Preparedness and Response
- BARDA: Biomedical Advanced Research & Development Authority
- CDC: Centers for Disease Control and Prevention
- FDA: Food and Drug Administration
- NIH: National Institutes of Health
Enterprise Approach
Sources of Federal Legal Preparedness Authorities for MCMs

- Pandemic and All-Hazards Preparedness Reauthorization Act (PAHPRA) (2013) (PL 113-5)
Why are legal/regulatory mechanisms for emergency use of MCMs needed?

• Without these mechanisms, certain preparedness and response activities at the local, state, and/or federal levels could otherwise violate provisions of the FD&C Act (e.g., render a product unapproved, adulterated, or misbranded):
  
  – Some MCMs needed for a response might not yet be approved, licensed, or cleared by FDA (e.g., Ebola, Zika, nerve agents)

  – Some MCMs needed for a response might be approved by FDA, but not for a specific emergency use (e.g., for a new indication)

  – Some MCMs might be approved for the emergency use, but:
    • Need to be dispensed without individual patient prescriptions (e.g., at points of dispensing (PODs)), by someone who is not a licensed health care professional, with streamlined instructions/fact sheets tailored for the emergency, and/or beyond the manufacturer-labeled expiration date

• Also, to ensure that available HHS Public Readiness and Emergency Preparedness (PREP) Act protections apply
FDA Authorities to Facilitate Access to MCMs in Response to Emergencies

• Emergency Use Authorization (EUA)
  – FD&C Act § 564
  – Established by Project BioShield Act (2004); amended by PAHPRA (2013), Cures Act (2016), and PL 115-92 (2017)

• Other MCM emergency use authorities
  – FD&C Act §§ 564A, 505-1, and 564B
  – Emergency dispensing orders, expiry dating extensions, waivers of Current Good Manufacturing Practice (CGMP) and Risk Evaluation and Mitigation Strategy (REMS) requirements, and government stockpiling (FDA); emergency use instructions (EUI) (delegated to CDC)
  – Established by PAHPRA (2013); amended by Cures Act (2016)

• 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
  – Amended by:
    • PAHPRA (2013) (to provide additional EUA flexibilities),
    • Cures Act (2016) (to add animal drugs), and
    • PL 115-92 (2017) (to provide additional EUA flexibilities and enhance FDA-Department of Defense (DoD) engagements)

• With an EUA, FDA can authorize for use in emergencies involving a CBRN agent(s) (and, for DoD, an agent(s) of war):
  – The use of unapproved MCMs or
  – The 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; an EUA can also help to ensure applicable PREP Act coverage is available
EUA Authority Amendment: PL 115-92

- Enacted December 12, 2017 (H.R. 4374)
- Amended section 564 of the FD&C Act to authorize additional emergency uses of medical products for threats (i.e., in addition to CBRN agents) to include “an agent or agents that may cause, or are otherwise associated with, an imminently life-threatening and specific risk to United States military forces”
- Also authorizes DoD to request, and FDA to provide, assistance to expedite development and review of products to diagnose, treat, or prevent serious or life-threatening diseases or conditions facing U.S. military forces
- January 16, 2018: FDA and DoD announced the launch of a joint program to prioritize the efficient development of safe and effective medical products intended for deployed U.S. military forces, including an “Initial Work Plan for Products Relevant to DoD”
EUA Authority

- EUA requests are typically submitted by government partners (e.g., CDC, ASPR, DoD) or industry sponsors; FDA may prioritize requests if needed

- Overview of requirements/steps for EUA issuance:

  1. Secretary of Department of Homeland Security (DHS), Health and Human Services (HHS), or DoD makes a specific type of determination (actual or potential emergency/threat):
     - **DHS**: Domestic emergency involving CBRN agent(s) or material threat determination (MTD),
     - **HHS**: Public health emergency involving CBRN agent(s), or
     - **DoD**: Military emergency involving a CBRN agent(s) or an agent(s) of war

  2. HHS Secretary issues a declaration (“EUA declaration”) that circumstances exist to justify EUA issuance based on 1 of the 4 types of determinations listed above *(this is *not* a PHS Act § 319 Public Health Emergency (PHE) declaration)*

  3. FDA ensures EUA criteria for issuance are met and issues the EUA when appropriate
Summary of Process for EUA Issuance

In the case of a DoD Secretary determination, the HHS Secretary shall determine within 45 days whether to issue an EUA declaration.
EUA Criteria for Issuance

• Criteria for issuance are based on the totality of scientific evidence available to FDA:

  – Serious or life-threatening illness/condition caused by the agent(s) referred to in the HHS Secretary’s EUA declaration

  – Reasonable belief the product “may be effective” in preventing, diagnosing, or treating serious or life-threatening diseases or conditions caused by the agent(s) (or mitigating a disease or condition caused by an FDA-regulated product used to diagnose, treat, or prevent a disease or condition caused by the agent(s))

  – Known/potential benefits outweigh known/potential risks

  – No adequate, approved, and available alternative to the product
EUA Evidence of Effectiveness

• “May be effective”
• Provides for a lower level of evidence than the "effectiveness" standard FDA uses for product approvals
• FDA intends to assess the potential effectiveness of a possible EUA product on a case-by-case basis using a risk-benefit analysis (next slide)
• If, based on the totality of the scientific evidence available, it is reasonable to believe that the product may be effective for the specified use, FDA may authorize its emergency use, provided that other statutory criteria for issuing an EUA also are met
• The amount, type, and quality of evidence available to support an EUA may not always be the same as that required for expanded access, IDEs, or humanitarian device exemptions under the FD&C Act and FDA regulations
EUA Risk/Benefit Analysis

• FDA must take into consideration the material threat posed by the agent(s) identified in the HHS Secretary’s EUA declaration if applicable (section 564(c))

• In determining whether the known and potential benefits of the product outweigh the known and potential risks, FDA intends to look at the totality of the scientific evidence to make an overall risk-benefit determination
  – Such evidence could arise from a variety of sources and may include (but is not limited to): results of domestic and foreign clinical trials, *in vivo* efficacy data from animal models, and *in vitro* data

• FDA will also assess the quality and quantity of the available evidence, given the current state of scientific knowledge

• The types of evidence that FDA may consider and that should be submitted to support a request for an EUA are discussed in section III.D.2 of the EUA guidance
EUA Conditions of Authorization

• Safeguards included in, and specific to, each EUA. Some are required, while some are discretionary to protect the public health. For example:
  – Information on emergency use (e.g., fact sheets for product recipients and for health care professionals)
    • e.g.) notification that the product is being used under an EUA and is not FDA-approved
  – Dispensing/screening procedures
  – Record keeping and monitoring of adverse events
  – Collection of information
  – Roles (e.g., for DoD, health care professionals, laboratories, etc.)
  – Advertising and promotion
EUA Package

• An EUA package consists of:
  – A letter of authorization and
  – Any accompanying materials (e.g., fact sheets for health care professionals, fact sheets for patients/recipient, instructions for use, labels)

• Made available publicly on the FDA website and in the Federal Register

• May be amended
Example of EUA Issuance Process:
Rafa Atropine Auto-Injector

- March 9, 2017: CDC requested an EUA for the 2 mg Atropine Auto-Injector manufactured by Rafa Laboratories Ltd. for the initial treatment of muscarinic symptoms of poisoning by susceptible nerve agents (NA) or certain insecticides (organophosphorus and/or carbamate)

- April 11, 2017:
  - HHS Secretary determined under section 564 of the FD&C Act that there is a significant potential for a public health emergency that has a significant potential to affect national security or the health and security of U.S. citizens living abroad and that involves nerve agents or certain insecticides (organophosphorus and/or carbamate)

  - Based on the above determination, the HHS Secretary declared under section 564 that circumstances exist justifying the authorization of the emergency use of injectable treatments for nerve agent or certain insecticide (organophosphorus and/or carbamate) poisoning, subject to the terms of any EUA issued

    - This declaration is not limited to the Rafa product; it was drafted to be flexible in anticipation of possible additional EUAs for other injectable NA treatments
Example of EUA Issuance Process: Rafa Atropine Auto-Injector (cont.)

• **April 11, 2017**: FDA issued an **EUA** for the Rafa Atropine Auto-Injector (2 mg) (this is the 1st EUA for a nerve agent product)

• **May 4, 2017**: HHS Secretary issued a **PREP Act Declaration** to provide liability protections for MCMs against nerve agents and certain insecticides (the effective date is April 11, the same date of issuance of as the Rafa EUA)

• **May 23, 2017**: Per CDC request and FDA review of data, FDA issued a **Letter Granting EUA Amendment** to authorize (1) use of 0.5 mg and 1 mg (i.e., pediatric) strengths and (2) use of revised fact sheets

• **January 24, 2018**: Per CDC request and FDA review of data, FDA issued another **Letter Granting EUA Amendment** to authorize (1) administration through clothing and (2) certain manufacturing changes

• Rafa EUA, Letters Granting EUA Amendment, HHS Nerve Agent Determination/Declaration, and PREP Act Declaration are available at:
  - [https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm#nerveagents](https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm#nerveagents)
FACT SHEET FOR PATIENTS AND CAREGIVERS: Use of the Rafa Atropine Auto-Injector for Initial Treatment of Nerve Agent or Certain Insecticide (Organophosphorus and/or Carbamate) Poisoning

You are being given the Rafa Atropine Auto-Injector because you or someone you know may have been exposed to nerve agents or certain insecticides (organophosphorus and/or carbamate) that could cause injury, harm, or death. These nerve agents or insecticides attack the central nervous system, the part of your body that controls your brain, spinal cord, and nerves. These nerve agents or insecticides can be a liquid, gas, or solid. As little as one drop of some nerve agents on your skin can cause death within 15 minutes of contact.

Atropine is used as the initial treatment for symptoms of nerve agent or certain insecticide poisoning. The Rafa Atropine Auto-Injector, which contains atropine, is being made available to treat poisoning by nerve agents or certain insecticides (organophosphorus and/or carbamate). This medicine may increase your chance of survival after coming in contact with these nerve agents or certain insecticides.

This Fact Sheet contains:
A. Information to help you understand the risks and benefits of the Rafa Atropine Auto-Injector you have received or may receive.
B. Instructions on how you or a caregiver can give (administer) the Rafa Atropine Auto-Injector in an emergency if a healthcare provider is not available to administer it.

A. INFORMATION ABOUT THE RISKS AND BENEFITS OF THE RAFA ATROPINE AUTO-INJECTOR

What is atropine and what is the Rafa Atropine Auto-Injector?
Atropine is a medicine to help reduce or block the effects of nerve agent or certain insecticide poisoning (organophosphorus and/or carbamate). This medicine comes in a self-containing device (auto-injector) which gives only a single dose by injection (shot) into the outer thigh. The needle that springs out of the device to deliver a single dose cannot be drawn back and the device cannot be reused. Each injector called the Rafa Atropine Auto-Injector is made to self-administer or administer the medicine to another person. The Rafa Atropine Auto-Injector is available in these doses that are administered based on a person’s weight or age: 0.5 mg, 1 mg, or 2 mg. The different auto-injector doses are color-coded, as shown below. See Table 1 for selecting the correct dose based on a person’s weight (or age if the weight is not known).

![Image showing 0.5 mg, 1 mg, and 2 mg Atropine Auto-Injectors]

Who can receive the Rafa Atropine Auto-Injector?
The Rafa Atropine Auto-Injector should be administered only to adults and children weighing 15 lbs (7 kg) or more (generally 6 months of age and older) who have been exposed to nerve agents or certain insecticides and are experiencing symptoms of nerve agent or insecticide poisoning. See Table 2 below for symptoms of nerve agent or insecticide poisoning.

What are the symptoms of nerve agent or insecticide poisoning?
Symptoms of nerve agent or insecticide poisoning may include nausea, vomiting, stomach cramps, inability to control urine and/or stool, confusion, muscle twitching or weakness, and convulsions (seizures). The number of Rafa Atropine Auto-Injectors needed depends on how mild or severe the symptoms are. See Table 2 below for mild or severe symptoms of nerve agent or certain insecticide (organophosphorus and/or carbamate) poisoning.

https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm182568.htm#nerveagents
Figure 1. Instructions on how to administer Rafa Atropine Auto Injector to yourself or others

A.) Confirm you have the correct dose based on weight or age (see Table 1). Hold the plastic sleeve on both sides of the perforation and tear apart at edge to open. Remove the auto-injector from the plastic sleeve. Be careful not to place fingers on the green tip.

B.) Firmly hold the auto-injector with the green tip pointed down.

C.) Pull off the yellow safety cap with your other hand.

D.) Aim and firmly jab the green tip straight down (a 90° angle) against the outer thigh. The auto-injector device will give the medicine when you do this. You can inject through clothing, but make sure pockets at the injection site are empty.

*Infants, small children, and adults who may not have a lot of fat at the injection site should also be injected in the thigh, but before giving the injection, bunch up the thigh to provide a thicker area of injection.

E.) Hold the auto-injector firmly in place for at least 10 seconds to allow the injection to finish.

F.) After 10 seconds, remove the auto-injector from the thigh (or from the thigh of the individual to whom you are administering the auto-injector) and massage the injection site in a circular motion for several seconds.

Note: If you do not see the needle visible after removal from the thigh it means an injection did not occur. Check to be sure the yellow safety cap has been removed. After yellow safety cap removal has been verified, repeat steps D and E pressing harder against the thigh to activate the injector. If you still do not see the needle, use a new auto-injector and start over again at step A.
List of EUAs Issued
# EUAs Issued by FDA

<table>
<thead>
<tr>
<th>Year</th>
<th>MCM</th>
<th>Requester</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anthrax (Bacillus anthracis)</strong></td>
<td></td>
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<tr>
<td>2005</td>
<td>Anthrax Vaccine Adsorbed (AVA)</td>
<td>DoD</td>
<td>Terminated</td>
</tr>
<tr>
<td>2011</td>
<td>Doxycycline (oral forms) for mass dispensing</td>
<td>HHS (CDC)</td>
<td>Current*</td>
</tr>
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</table>

| **H1N1 Influenza Pandemic (2009)** |                                  |                       |                              |
| 2009-2010          | Antivirals (3)                     | HHS (CDC)            | Terminated (all H1N1 EUAs)   |
|                    | IVDs (18)                          | Various              |                              |
|                    | Disposable N95 respirators         | HHS (CDC)            |                              |

| **H7N9 Influenza** |                                                   |                       |                              |
| 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 Corp.         | Current                      |
| 2014              | A/H7N9 Influenza Rapid Test                 | Arbor Vita Corp.     | Current                      |

| **Middle East Respiratory Syndrome Coronavirus (MERS-CoV)** |                          |                       |                              |
| 2013 (reissued 2014) | CDC Novel Coronavirus 2012 Real-time RT-PCR Assay | HHS (CDC)            | Current                      |

- To be terminated due to April 2016 issuance of doxycycline emergency dispensing order, CGMP waiver, and CDC EUI (under sec. 564A of the FD&C Act).
- For the most current FDA EUA information, see: www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm

Updated August 21, 2017
## EUAs Issued by FDA

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<tr>
<th>Year</th>
<th>MCM</th>
<th>Requester</th>
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<tr>
<td><strong>Ebola Virus</strong></td>
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<td>2014 (reissued 2014)</td>
<td>DoD EZ1 Real-time RT-PCR Assay</td>
<td>DoD</td>
<td>Current</td>
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<tr>
<td>2014 (reissued 2015)</td>
<td>CDC Ebola VP40 rRT-PCR Assay</td>
<td>HHS (CDC)</td>
<td>Current</td>
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<td>2014 (reissued 2015)</td>
<td>CDC Ebola NP rRT-PCR Assay</td>
<td>HHS (CDC)</td>
<td>Current</td>
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<td>2014 (reissued 2014)</td>
<td>FilmArray NGDS BT-E Assay</td>
<td>BioFire Defense, LLC</td>
<td>Current</td>
</tr>
<tr>
<td>2014 (reissued 2015)</td>
<td>FilmArray Biothreat-E test</td>
<td>BioFire Defense, LLC</td>
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<tr>
<td>2014 (reissued 2014)</td>
<td>RealStar Ebolavirus RT-PCR Kit 1.0</td>
<td>altona Diag. GmbH</td>
<td>Current</td>
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<tr>
<td>2014</td>
<td>LightMix Ebola Zaire rRT-PCR Test</td>
<td>Roche Molecular Systems, Inc.</td>
<td>Current</td>
</tr>
<tr>
<td>2015 (reissued 2016)</td>
<td>ReEBOV Antigen Rapid Test</td>
<td>Zalgen Labs, LLC</td>
<td>Current</td>
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<tr>
<td>2015</td>
<td>Xpert Ebola Assay</td>
<td>Cepheid</td>
<td>Current</td>
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<tr>
<td>2015</td>
<td>OraQuick Ebola Rapid Antigen Test</td>
<td>OraSure Technologies, Inc.</td>
<td>Current</td>
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<tr>
<td>2016</td>
<td>Idylla Ebola Virus Triage Test</td>
<td>Biocartis NV</td>
<td>Current</td>
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<tr>
<td><strong>Enterovirus D68 (EV-D68)</strong></td>
<td>CDC EV-D68 2014 rRT-PCR Assay</td>
<td>HHS (CDC)</td>
<td>Current</td>
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<tr>
<td><strong>Nerve Agents</strong></td>
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<tr>
<td>2017 (amended 2017, 2018**)</td>
<td>2 mg Atropine Auto-Injector</td>
<td>CDC</td>
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**On May 23, 2017, at CDC’s request, FDA issued an EUA amendment to authorize (1) use of pediatric strengths (i.e., 0.5 mg and 1 mg) of the Rafa Atropine Auto-Injector, in addition to the 2 mg strength, and (2) updates to the original fact sheets to include all three strengths. On January 24, 2018, at CDC’s request, FDA issued an EUA amendment to authorize (1) administration through clothing and (2) certain manufacturing changes.**

*Updated January 24, 2018*
<table>
<thead>
<tr>
<th>Year</th>
<th>MCM</th>
<th>Requester</th>
<th>Status</th>
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<tbody>
<tr>
<td>2016 (amended 2016 &amp; 2017)</td>
<td>CDC Zika MAC-ELISA (IgM)</td>
<td>HHS (CDC)</td>
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<td>2016 (amended 2016 &amp; 2017)</td>
<td>Zika Virus RNA Qualitative Real-Time RT-PCR</td>
<td>Quest Diagnostics Infectious Disease, Inc.</td>
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<td>2016 (amended 2017)</td>
<td>Zika Virus Real-time RT-PCR Test</td>
<td>Viracor Eurofins</td>
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<td>2016 (amended 2016)</td>
<td>VERSANT® Zika RNA 1.0 Assay (kPCR) Kit</td>
<td>Siemens Healthcare Diagnostics Inc.</td>
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<tr>
<td>2016 (amended 2017)</td>
<td>xMAP® MultiFLEX™ Zika RNA Assay</td>
<td>Luminex Corporation</td>
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</tr>
<tr>
<td>2016 (amended 2017)</td>
<td>ZIKV Detect™ IgM Capture ELISA</td>
<td>InBios International, Inc.</td>
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<td>2016</td>
<td>Sentosa® SA ZIKV RT-PCR Test</td>
<td>Vela Diagnostics USA, Inc.</td>
<td>Current</td>
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<td>2016</td>
<td>Zika Virus Detection by RT - PCR Test</td>
<td>ARUP Laboratories</td>
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<td>2016</td>
<td>Zika ELiTe MGB® Kit U.S.</td>
<td>ELITechGroup Inc. Molecular Diagnostics</td>
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<tr>
<td>2017</td>
<td>Gene-RADAR® Zika Virus Test</td>
<td>Nanobiosym Diagnostics, Inc.</td>
<td>Current</td>
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<tr>
<td>2017</td>
<td>LIAISON® XL Zika Capture IgM Assay</td>
<td>DiaSorin Incorporated</td>
<td>Current</td>
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<td>2017</td>
<td>TaqPath Zika Virus Kit (ZIKV)</td>
<td>Thermo Fisher Scientific</td>
<td>Current</td>
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<td>2017</td>
<td>CII-ArboViroPlex rRT-PCR</td>
<td>Columbia University</td>
<td>Current</td>
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<td>Year</td>
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<td>2017</td>
<td>ADVIA Centaur Zika test</td>
<td>Siemens Healthcare Diagnostics Inc.</td>
<td>Current</td>
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<tr>
<td>2017</td>
<td>DPP Zika IgM Assay System</td>
<td>Chembio Diagnostic Systems, Inc.</td>
<td>Current</td>
</tr>
</tbody>
</table>

Zika Virus (cont.)

Updated September 27, 2017
Other MCM Emergency Use Authorities
Other MCM Emergency Use Authorities

- Established by PAHPRA (2013); amended by 21st Century Cures Act (2016)

- For MCMs that are FDA-approved/cleared for CBRN use, to facilitate stakeholder preparedness and response without EUA issuance, while preserving applicable PREP Act protections (FD&C Act § 564A)
  - Emergency dispensing orders (FDA)
  - Emergency use instructions (EUI) (CDC)
  - Expiration dating extensions (FDA)
  - CGMP waivers (FDA)
  - REMS waivers (FDA)

- Pre-positioning (FD&C Act § 564B)
  - PAHPRA allows for pre-positioning of approved/unapproved MCMs by or on behalf of government entities (federal, state, local) in anticipation of FDA approval, clearance, licensure or EUA or IND issuance
  - But, the MCM may not be used until it is approved or authorized for emergency or investigational use
Overview of FDA Zika Virus Response
FDA advises testing for Zika virus in all donated blood in the U.S.

United States Government Zika Virus Disease Contingency Response Plan

September 2016

FDA is supporting Zika diagnostic test development.

Tests Needed

1. Diagnostic test
2. Baseline and follow-up

Types of Tests

- Rapid diagnostic test
- Virus isolation
- Antibody testing

CDC’s Response to Zika

When to Test for Zika

As a healthcare provider, you decide if a patient should be tested for Zika virus infection. The algorithm below will help you determine whether or not to test your patient for Zika virus infection. For information on which test to use, see CDC’s interim guidance.

1. If your patient is:
   - Experiencing or has recently experienced symptoms of Zika?
   - An asymptomatic pregnant woman?
   - Ask the following questions:

   NO
   - Does the patient live in or has the patient recently traveled to an area with Zika?
   - Has the patient had unprotected sex with a partner who has lived in or traveled to an area with Zika?

   YES
   - Test for Zika

Do Not Test for Zika

Healthcare providers should know that local and state health jurisdictional guidelines regarding testing of patients will usually override those within the test kit or label manuals.

CDC does not recommend Zika virus testing for asymptomatic:

- Man
- Children
- Women who are not pregnant

Revised Recommendations for Reducing the Risk of Zika Virus Transmission by Blood and Blood Components

Guidance for Industry

This guidance is for immediate implementation.

FDA is issuing this guidance for immediate implementation in accordance with 21 CFR 10.11(g)(2) without initially seeking prior comment because the agency has determined that prior public participation is not feasible or appropriate.

Considerations for Developing a Zika Virus Vaccine

The rapid spread of Zika virus through the Americas and its debilitating consequences for pregnant women and infants have precipitated an international, multiagency response. Numerous countries are taking steps to address the need for vaccines, and the U.S. has allocated substantial resources to support vaccine development and research.

Hilary D. Marston, M.D., M.P.H., Nicole Luong, M.D., M.S.P.H., Jessica L. Beers, M.D., and Anthony S. Fauci, M.D.

Perspective

September 2016
FDA Zika Virus Response

- FDA has been fully engaged with USG and other partners in responding to the Zika virus outbreak
- No FDA-approved, -licensed, or -cleared vaccines, treatments, or diagnostic tests to prevent, treat, or diagnose Zika virus available
- One FDA-approved test for screening Zika virus in blood donations
  - Intended for use by blood collection establishments to detect Zika virus in blood donations, not for individual diagnosis of Zika virus infection (October 2017)
- Prepared to leverage our authorities to help accelerate the development and availability of safe and effective medical products for Zika virus
- Primary areas of activity have included:
  1. Blood safety
  2. Clinical diagnostic tests
  3. Vaccine and therapeutic development
  4. Vector control
  5. Fraudulent product monitoring

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MCM Monitoring and Assessment: Beyond the Last Mile
FDA’s MCM Roles

• Facilitating development of and access to safe and effective MCMs

• Legal mechanisms (e.g., EUA, IND, IDE, Expanded Access)

• Consumer protection

• Collaboration

• **Monitoring MCM use for safety and effectiveness**
Public Health Emergencies: CBRN & EID

Chemical + Biological + Radiological + Infectious Diseases

Source: HHS/ASPR.
The U.S. government has a limited capacity to rapidly collect and analyze public health emergency (PHE) MCM safety and effectiveness data, especially during a PHE response.

...now what?
External Partners and Stakeholders

- NGOs & Think Tanks
- International
- State & Local
- Academia
- Public
- Industry
- Academia
- Public
- Industry
- NGOs & Think Tanks
- International
- State & Local

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M&A Issues

- Regulatory science & regulatory policy
- Emergency preparedness and response
- Technical, administrative, legal, and logistical challenges
How is assessment different in a public health emergency?

<table>
<thead>
<tr>
<th>PHE</th>
<th>TRADITIONAL R&amp;D</th>
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<tbody>
<tr>
<td>• Intent – respond and mitigate</td>
<td>• Intent – generalizable knowledge</td>
</tr>
<tr>
<td>• Unplanned / Unexpected</td>
<td>• Planned / Deliberate</td>
</tr>
<tr>
<td>• Uncontrolled or no data collection</td>
<td>• Well-controlled clinical trials</td>
</tr>
<tr>
<td>• Undefined number of individuals</td>
<td>• Defined number of individuals</td>
</tr>
<tr>
<td>• Simultaneous administration / multiple products</td>
<td>• Stepwise progression / single product administration</td>
</tr>
<tr>
<td>• Requires rapid decision-making</td>
<td>• Allows more time for decision-making</td>
</tr>
<tr>
<td>• Little or no tracking / monitoring</td>
<td>• Strict oversight and monitoring</td>
</tr>
<tr>
<td>• Lack of / limited clinical provider oversight</td>
<td>• Principal investigator / clinical study staff interaction</td>
</tr>
<tr>
<td>• Limited reporting and information dissemination</td>
<td>• Informed consent/IRB</td>
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<td></td>
<td>• Clearly defined reporting requirements and information sharing</td>
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[www.fda.gov](http://www.fda.gov)
Progress to Date

CIADMs

Fill Finish Mfg. Network

FADG

Nonclinical Development Network

Regulatory & Quality Affairs

2006

2012

2013

2009

2011

2014

BARD

Image courtesy of BARDA.

www.fda.gov
Recent M&A Activities

- National Academies of Sciences, Engineering, and Medicine (NASEM) Workshop (June 6-7, 2017)
  - Building a National Capability to Monitor and Assess Medical Countermeasure Use During a Public Health Emergency: Going Beyond the Last Mile: Proceedings of a Workshop

- PHEMCE MCM Monitoring and Assessment Integrated Program Team (IPT)

- Patient-Centered Outcomes Research Trust Fund (PCORTF)

- FDA’s Real-Time Application for Portable Interactive Devices (RAPID) System

- FDA Sentinel Initiative
Looking Ahead...
Additional Resources

- FDA Medical Countermeasures Initiative (MCMi)
  - www.fda.gov/medicalcountermeasures

- FDA EUA Website *(official updates, current & terminated EUAs, guidance)*
  - www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm

- Final Guidance on EUAs & Other MCM Emergency Use Authorities

- MCM Emergency Use Authorities Website

- MCM Monitoring and Assessment
  - https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm561377.htm

- FDA Zika Response Updates Website
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMIssues/ucm485199.htm

- PL 115-92 (H.R. 4374) *(including Initial Work Plan issued on January 16, 2018)*
  - https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm2007271.htm#PL11592

- 21st Century Cures Act: MCM-Related Provisions *(including MCM PRVs)*
  - https://www.fda.gov/EmergencyPreparedness/Counterterrorism/MedicalCountermeasures/MCMLegalRegulatoryandPolicyFramework/ucm566498.htm
Thank you!

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