



# Treating Influenza and Emerging Diseases - Challenge to Industry

Melissa Willis, PhD  
Chief, Therapeutics Branch  
Influenza and Emerging Diseases Division

**BARDA Industry Day**  
**November 7, 2017**



# Challenge to Industry

How can industry help us address some of the major gaps we have when it comes to treating patients infected with influenza and emerging diseases?





# Influenza: A Formidable Threat

## Public Health Impact of Influenza

### Seasonal Influenza in U.S., Each Year



5%–20%  
U.S.  
Population  
Infected



\$10.4 Billion  
Medical  
Costs



\$87.1 Billion  
Economic  
Burden

### Severity Can Vary

2013-14  
U.S. Influenza Season



400K Hospitalizations  
(>200k pediatric  
and elderly)



13.5K Deaths

2014-15  
U.S. Influenza Season



700K Hospitalizations



19.5K Deaths

### Pandemic Influenza Threat

#### 1918 Pandemic

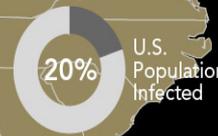


25%  
U.S.  
Population  
Infected



75M International  
Deaths    675.5K U.S.  
Deaths

#### 1957 Pandemic



20%  
U.S.  
Population  
Infected



70K  
U.S. Deaths

1.1M  
International  
Deaths

#### 1968 Pandemic



30%  
U.S.  
Population  
Infected



34K  
U.S. Deaths

1M  
International  
Deaths

#### 2009 Pandemic



20%  
U.S.  
Population  
Infected

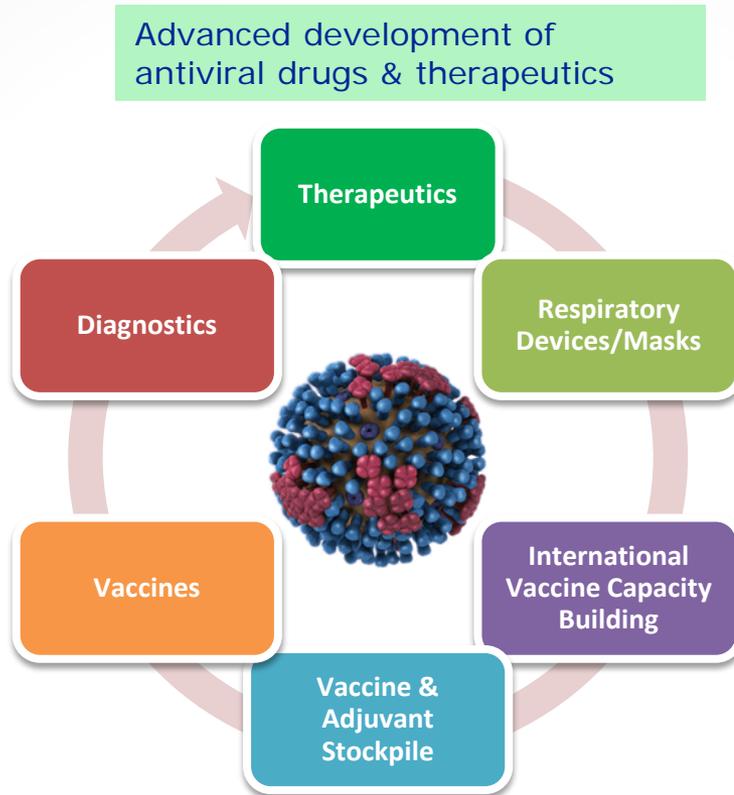


12.5K  
U.S. Deaths

203K  
International  
Deaths



# BARDA Pandemic Influenza Strategy



Advanced development of antiviral drugs & therapeutics

Develop rapid, near-patient diagnostics

Develop low cost, easy to use ventilators suitable for all ages with universal components

Develop reusable masks and respirators to address surge need during a pandemic

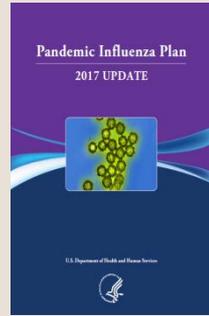
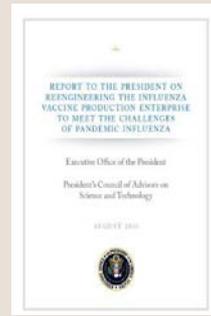
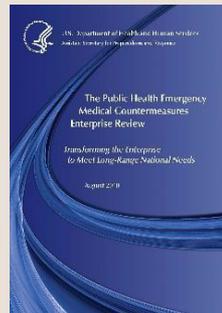
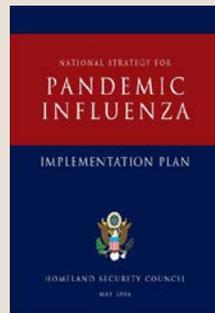
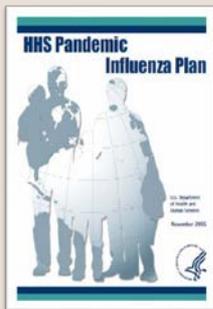
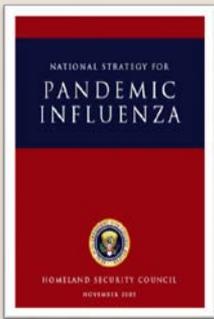
Provide pandemic vaccine for U.S. within 6 months (or less) of a pandemic declaration (600M doses)

Develop influenza vaccines that induce broader, longer duration of immunity

Enable 500M doses of pandemic vaccine production capacity in developing countries

More, Faster, & Better!

Stockpile vaccines against influenza strains with pandemic potential



# H7N9 Threat and Preparation



**Biomedical  
Advanced  
Research and  
Development  
Authority**

## Conditions for a Pandemic



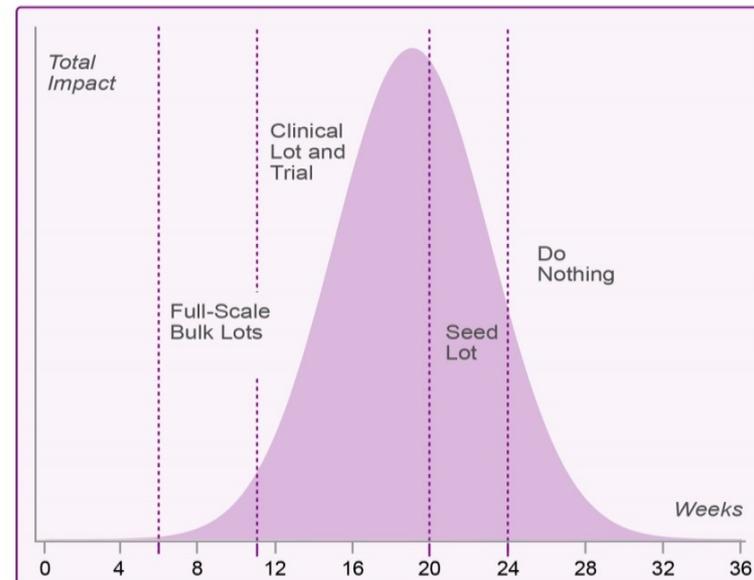
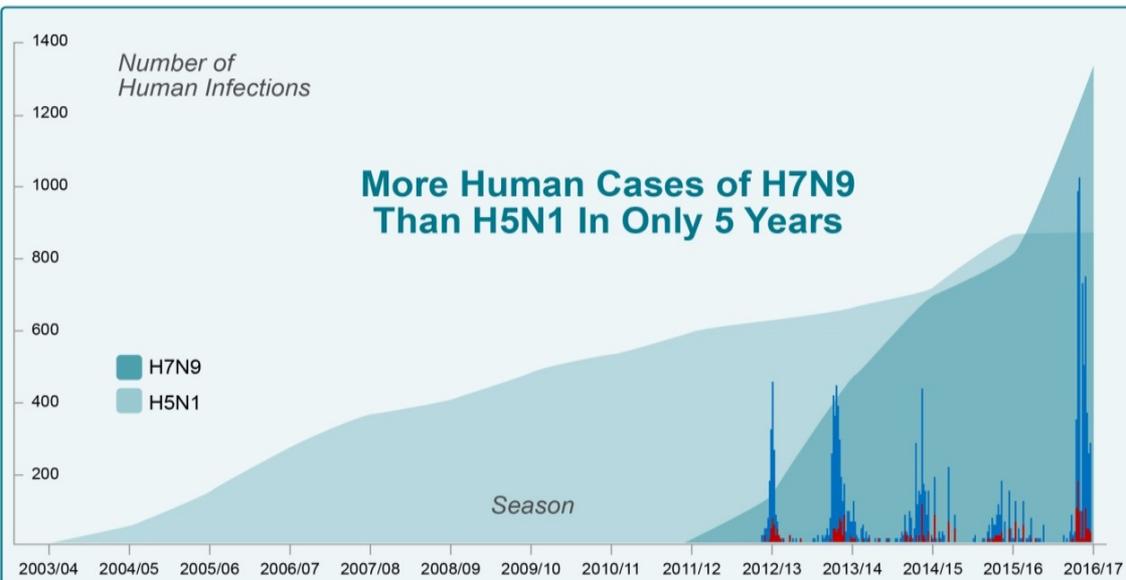
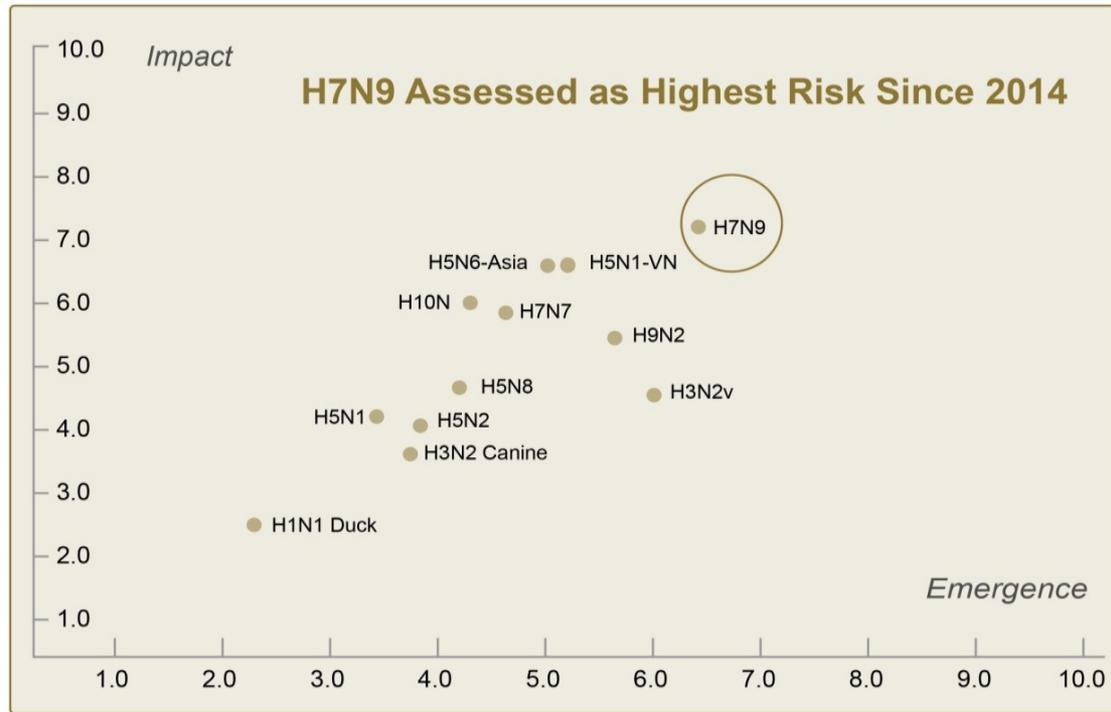
Novel Strain With  
Limited Prior Immunity  
in Population



Sustained  
Human-to-Human  
Transmission



Increased  
Geographic  
Spread





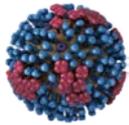
# Pandemic Preparedness – Antivirals

- **OLD WAY:** Pandemic preparedness = stockpiling drugs
- **NEW WAY:** Early use of antivirals saves lives
- **Industry Challenge:**
  - How can we reduce the barriers to early antiviral access?
    - Bringing influenza diagnostics closer to the patient to improve antiviral drug use and expedite detection of emerging pandemic viruses
    - Operational delivery - ease of use, single dose
  - Telemedicine
  - Disease tracking
    - Week behind → real-time → forecast



# Innovation in Influenza Identification

## Diagnostics and Access



**Leveraging home, wearable and POC diagnostics to enable early use of antiviral drugs could have a transformative impact**

### Closer to the patient

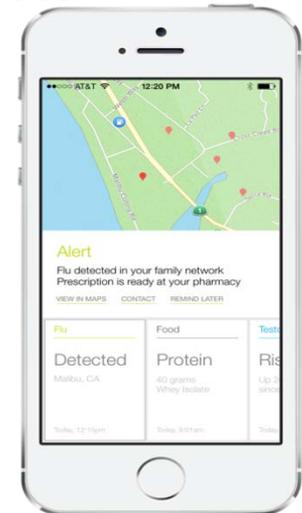
- Pre-symptom onset detection
- Wearable devices
- At home diagnostics

### Product innovation

- Product development and regulatory approval
- Ease of use

### Clinical benefit

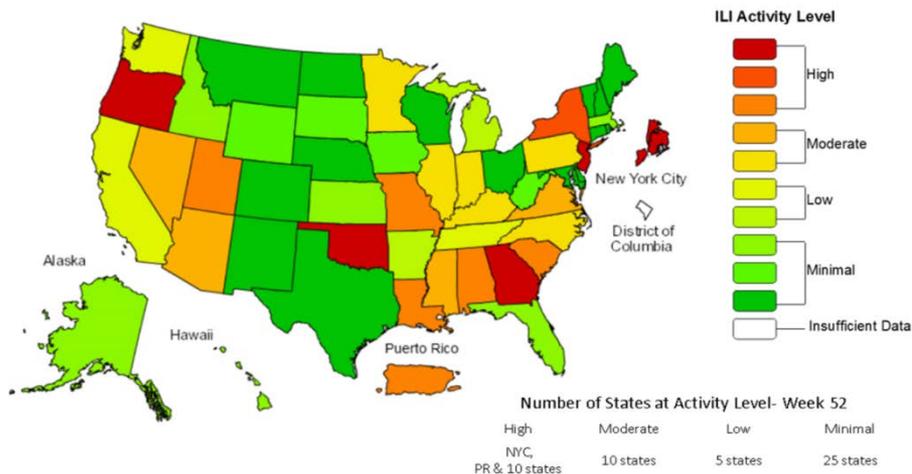
- Link early diagnostics with easy access to health care provider to yield antiviral intervention as early as possible



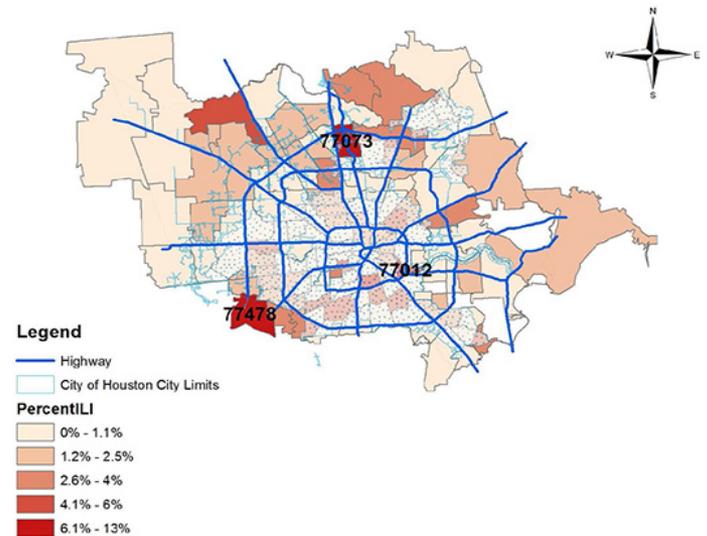


# Real Time Tracking of Influenza

**Influenza-Like Illness (ILI) Activity Level Indicator Determined by Data Reported to ILINet**  
**2016-17 Influenza Season Week 52 ending Dec 31, 2016**



Syndromic Surveillance: Geographic Distribution Map of ILI



During week 19, the ZIP codes that have the greatest percentage of ED visits related to ILI (6.0% or greater) are: 77012, 77073, and 77478

NOTE: Houston/Harris County ILI distribution map was created using data provided by 36 hospitals that voluntarily provide data based on chief complaints in the Real-time Outbreak Disease Surveillance System (RODS). This map reflects the percentage of ILI cases from each zip code from the total amount of cases seen in each zip code during the current week of reporting. Influenza-like illness (ILI) is defined as the mention of fever AND cough, OR fever AND sore throat, OR flu in the patient's ED chief complaint. These data do not represent laboratory confirmed cases of influenza nor do they represent all ED visits in Houston/Harris County.

Move to a more granular real-time analysis of influenza by linking de-identified diagnostic data to cloud based daily reporting

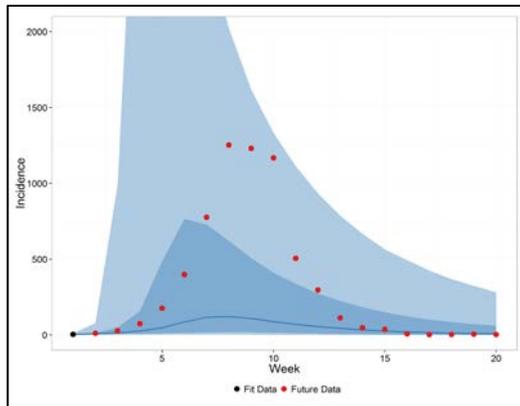




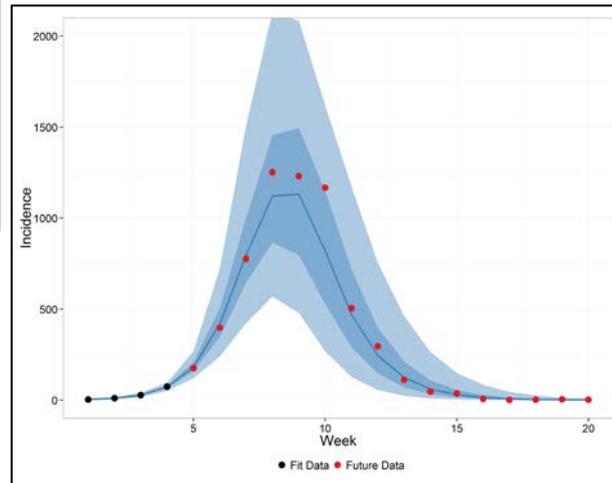
# Influenza Forecasting

For more information: Talk to Division of Quantitative Analysis and see BAA AOI #9 and #14.

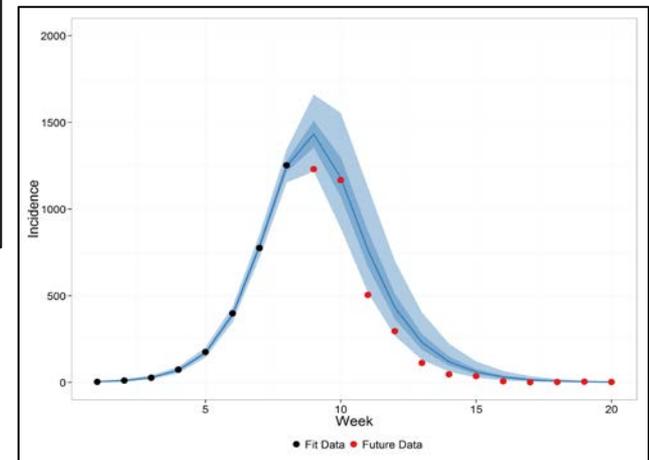
## 1 Week



## 4 Weeks



## 8 Weeks





# BAA Area of Interest #9.4

- **Real-time influenza tracking.**
  - Novel solutions that result in accurate, real-time influenza outbreak data down to the zip code level.....This data may also be used to develop models for influenza forecasting (See Area of Interest #14)
- **BARDA seeks data sets that measure the number of hospitalized influenza patients per hospital in a defined geographic area.**
  - down to the zip code level
  - cover the continental US
  - cover at least the last 5 northern hemisphere influenza seasons.
- **Better diagnostics and influenza tracking capabilities will improve our ability to execute clinical studies of new therapeutics in specific target populations.**

EFFICIENCY, SPEED, LOWER COST



# Available Influenza Treatments

## Acute Uncomplicated

- Oseltamivir
- Zanamivir
- Peramivir
- Laninamivir (Japan)
- Favipiravir (Japan-limited)
- Adamantanes

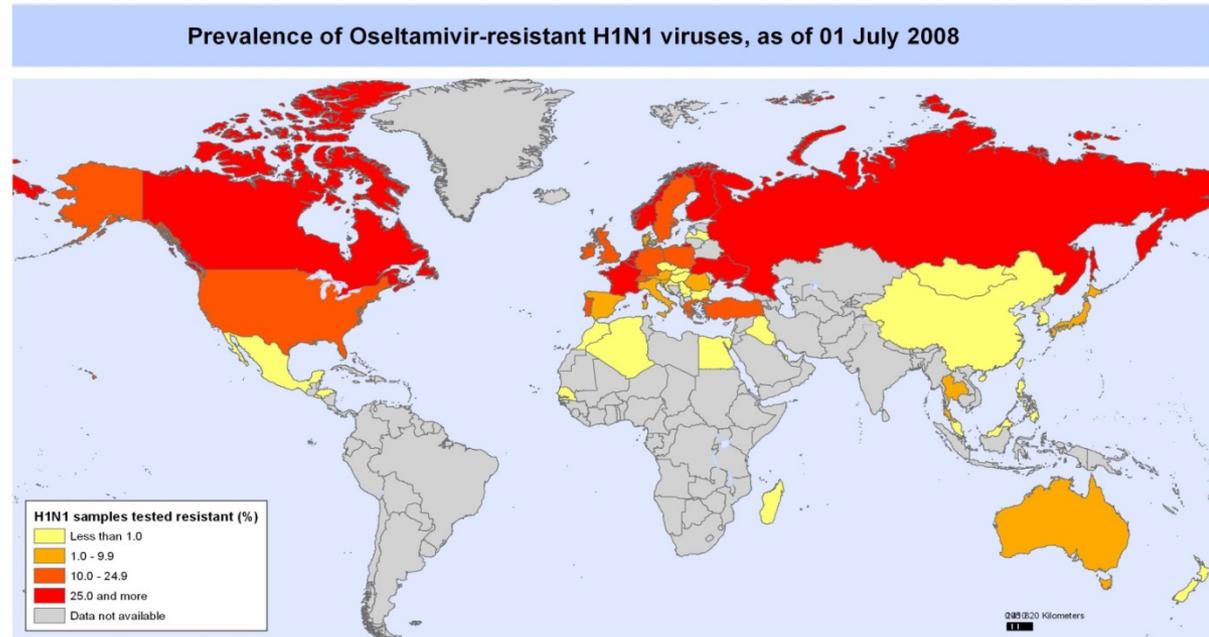
## Hospitalized, Severe

- No approved drugs for this indication in the U.S.



# Gaps to be Addressed

- Hospitalized
- NAI resistant strains – all populations
- Pediatrics
- Pregnant women



The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement.

Data Source: WHO/GIP  
Map Production: Public Health Information and Geographic Information Systems (GIS)  
World Health Organization



© WHO 2008. All rights reserved

[http://www.who.int/influenza/patient\\_care/antivirals/oseltamivir\\_summary/en/](http://www.who.int/influenza/patient_care/antivirals/oseltamivir_summary/en/)

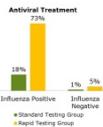


# Addressing Challenges

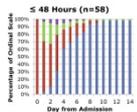
## Influenza Therapeutics



**BARDA is advancing strategic efforts that represent key gaps for pandemic preparedness**



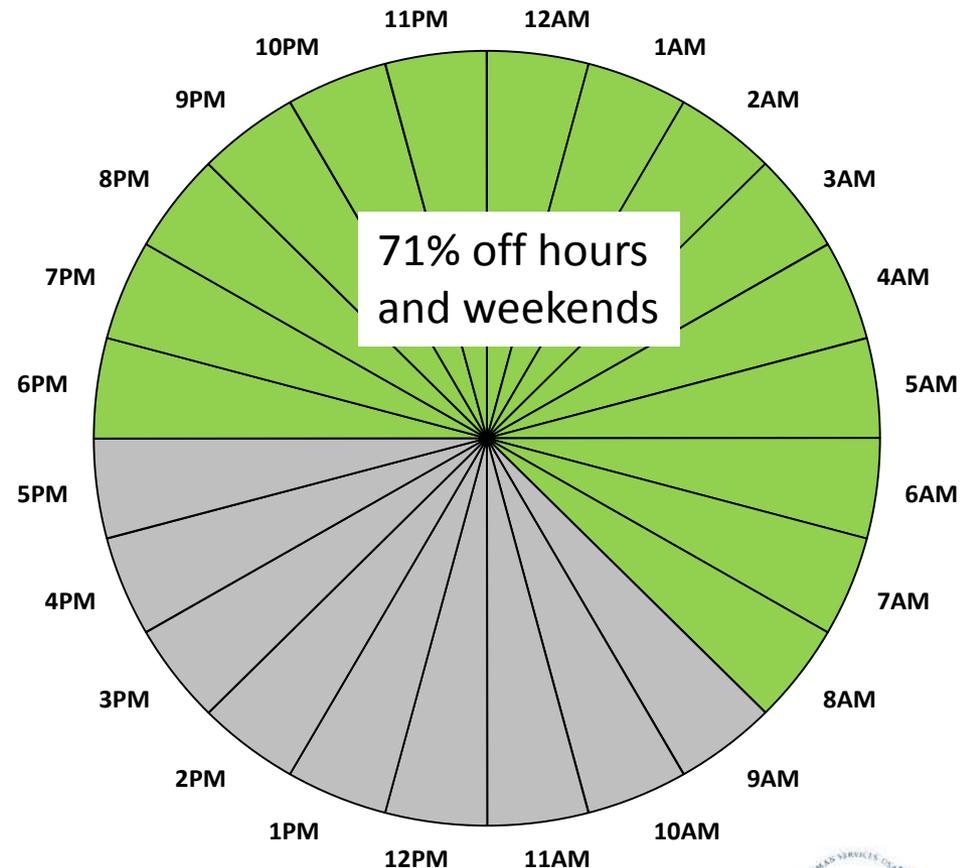
1. Disease tracking: inform epidemiology near real-time and maintain more-responsive position for improved site activation for ongoing trials and pandemic preparedness
2. Enrollment: leverage new tools and platforms to enhance clinical trial participation and operations, enhancing efficiency and effectiveness of clinical design, site-selection, and execution
3. Trial Design: key parameter for advancing innovative portfolio and addressing regulatory requirements
4. Endpoints: novel endpoints including composite and outcomes-based metrics to redefine the clinical paradigm for complicated influenza in the US





# Enrollment in Clinical Trials

- **OLD WAY:** Clinical study sites enroll on average one subject per site per season; Hospitalized influenza patients are a heterogeneous population resulting in huge variability in clinical trials
- **NEW WAY:** Use existing data to find geographic regions with above average influenza hospitalization rates; use EHR data to reduce heterogeneity by evaluating inclusion/exclusion criteria.
- **Challenge to Industry:** **INNOVATE** in the hospitalized clinical trial space! Adding more sites is not the solution to increasing enrollment!!!!





# Endpoints

- FDA Guidance for Industry – Influenza: Developing Drugs for Treatment and/or Prophylaxis (2011)
  - Primary Endpoint should include:
    - Clinical signs and symptoms
    - Duration of hospitalization
    - Time to normalization of vital signs
      - Fever
      - Respiratory status
      - Heart rate
      - Systolic blood pressure
    - Supplemental oxygenation requirements
  - Ordinal Scale
    - Discrete categories for classifying hospitalized subjects over time could include:
      - Death
      - ICU on mechanical ventilation
      - ICU
      - Hospital floor receiving supplemental oxygen
      - Hospital floor without supplemental oxygen
      - Discharge but has not returned to normal activity
      - Discharge returned to normal activity
    - Respiratory endpoint

**CHALLENGE: WHICH ONE IS THE BEST ONE?**



**KEEP  
CALM  
AND  
ACCEPT  
The Challenge**

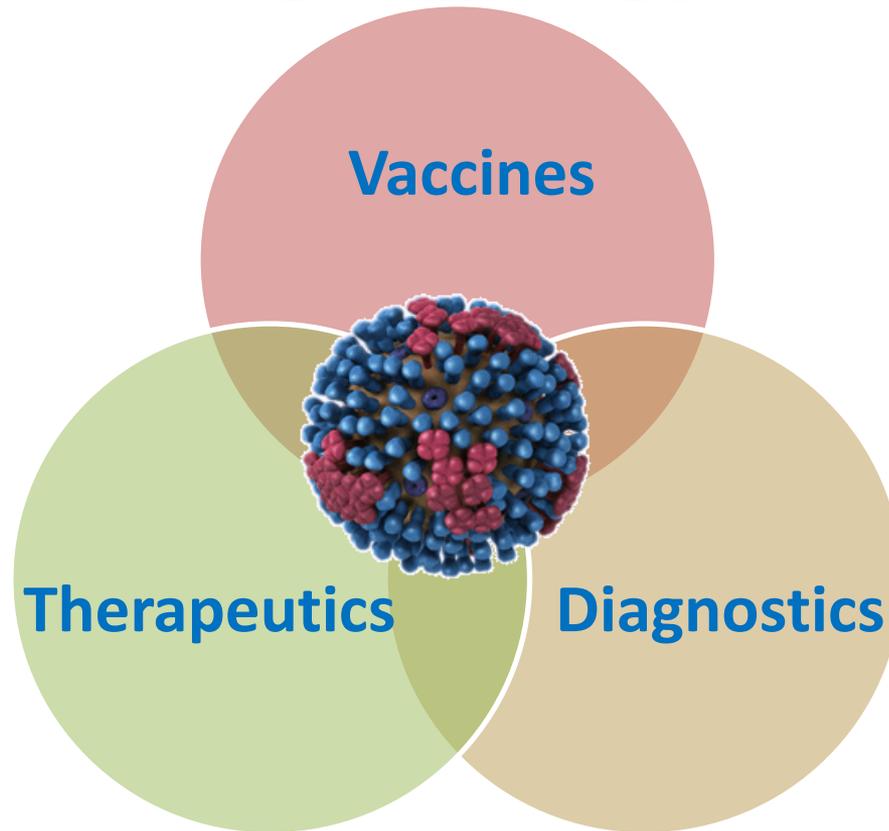


**Melissa.willis@hhs.gov**

[www.medicalcountermeasures.gov](http://www.medicalcountermeasures.gov)



# Influenza: An Integrated Response



Early Detection → Early Response → Saving Lives



# Online Resources

<https://www.medicalcountermeasures.gov/home.aspx>

- Portal to BARDA: Register to request a **TechWatch** meeting

<https://www.fbo.gov/> ("FedBizOpps")

- Official announcements and info for all government contract solicitations

<https://www.usajobs.gov/>

- Join the team!

<https://www.phe.gov/about/BARDA/Pages/default.aspx>

- Program description, information, news, announcements



Medical  
**Countermeasures.gov**



Public Health Emergency  
*Public Health and Medical Emergency Support for a Nation Prepared*

**USAJOBS**<sup>®</sup>  
"WORKING FOR AMERICA"