Treating Influenza and Emerging Diseases - Challenge to Industry

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ASPR: Saving Lives...Protecting America
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
- 1968 Pandemic
  - 30% U.S. Population Infected
  - 34K U.S. Deaths
  - 1M International Deaths
- 2009 Pandemic
  - 20% International Deaths
  - 12.5K U.S. Deaths
  - 203K International Deaths
BARDA Pandemic Influenza Strategy

- **Develop rapid, near-patient diagnostics**
- **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**
- **More, Faster, & Better!**

**Therapeutics**
- Advanced development of antiviral drugs & therapeutics
- Develop low cost, easy to use ventilators suitable for all ages with universal components

**Diagnostics**
- Develop rapid, near-patient diagnostics

**Respiratory Devices/Masks**
- Develop reusable masks and respirators to address surge need during a pandemic

**Vaccines**
- Stockpile vaccines against influenza strains with pandemic potential
- 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
- More, Faster, & Better!

**International Vaccine Capacity Building**
- Enable 500M doses of pandemic vaccine production capacity in developing countries

**Vaccine & Adjuvant Stockpile**
- Advanced development of antiviral drugs & therapeutics
- Develop low cost, easy to use ventilators suitable for all ages with universal components

**Develop near-patient diagnostics**
- More, Faster, & Better!
H7N9 Threat and Preparation

Conditions for a Pandemic

- Novel Strain With Limited Prior Immunity in Population
- Sustained Human-to-Human Transmission
- Increased Geographic Spread

More Human Cases of H7N9 Than H5N1 In Only 5 Years

H7N9 Assessed as Highest Risk Since 2014
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
Move to a more granular real-time analysis of influenza by linking de-identified diagnostic data to cloud-based daily reporting.

http://www.houstontx.gov/health/Epidemiology/flu_report.html
Influenza Forecasting

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

1 Week

4 Weeks

8 Weeks
- **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

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

CHALLENGE: WHICH ONE IS THE BEST ONE?
KEEP CALM AND ACCEPT The Challenge
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