BARDA’s Response to the Ebola Epidemic in West Africa
This is a PHEMCE and USG Response

- ASPR – Lead for PHEMCE activities and interactions with International Organizations
  - OEM – Lead for SOC activities
- CDC – Providing support for epidemiology, surveillance, and infection control
- FDA – Expediting review of INDs
- USAID – Supplies and medical personnel
- OPP – Coordinating activities with international partners
- NIH – Development of vaccines and therapeutics and clinical trials
- DoD – Development of vaccines and therapeutics, clinical trials, deploying mobile field hospitals
- BARDA – Development of therapeutics and vaccines
  - Programs will potentially transition to BARDA
  - Support activities for Phase 2 studies and other uses of candidate products (expanded access)
  - Coordinate use of CIADMs and Fill/Finish Network to assist developers
Ebola virus Background and Disease

• Ebola virus belongs to the family *Filoviridae*

• Five identified subspecies
  – Ebola virus (formally Zaire)
  – Sudan
  – Tai Forest
  – Bundibugyo
  – Reston

• Enveloped virus containing non-segmented, negative strand, RNA genome

• Symptoms appear 2 – 21 days after exposure, 8 – 10 days most common
  – Fever, severe headache, muscle pain, weakness, diarrhea, vomiting

• Advanced disease includes gastrointestinal bleeding, rash, and coagulation abnormalities

• Death attributed to diffuse internal bleeding and hypotensive shock

• There currently are no licensed/approved vaccines or treatments for Ebola
Ebola Virus Ecology

Enzootic Cycle
New evidence strongly implicates bats as the reservoir hosts for ebolaviruses, though the means of local enzootic maintenance and transmission of the virus within bat populations remain unknown.

Ebolaviruses:
- Ebola virus (formerly Zaire virus)
- Sudan virus
- Tai Forest virus
- Bundibugyo virus
- Reston virus (non-human)

Epizootic Cycle
Epizootics caused by ebolaviruses appear sporadically, producing high mortality among non-human primates and duikers and may precede human outbreaks. Epidemics caused by ebolaviruses produce acute disease among humans, with the exception of Reston virus which does not produce detectable disease in humans. Little is known about how the virus first passes to humans, triggering waves of human-to-human transmission, and an epidemic.

Human-to-human transmission is a predominant feature of epidemics.

Following initial human infection through contact with an infected bat or other wild animal, human-to-human transmission often occurs.
Ebola Virus Outbreaks in Africa
Historic and Current

3706 cases
1848 deaths
As of Sept. 4

Unrelated Outbreak
In DRC
62 cases as of Sept 10
Providing Care Under Extreme Conditions
Vaccines Under Development

• Due to the urgency, the FDA is expediting review of INDs to allow for evaluation in Phase 1 studies

• Vaccine Research Center (NIH) and GSK – ChimpAd3 vector vaccine
  – Currently in Phase 1 – bivalent vaccine (Zaire and Sudan) NIH
  – Currently in Phase 1 – monovalent (Zaire) UK
  – Additional monovalent vaccine being manufactured (Zaire)

• Newlink Genetics and Public Health Agency Canada – rVSV vector vaccine
  – Phase 1 to start in September – WRAIR (18-50yrs of age)
  – Phase 1 being planned at NIH – include patients above the age of 50
  – Phase 1 being discussed at NIH – HIV+ individuals
  – PHAC has pledged 800 doses to WHO

• Programs will potentially transition to BARDA to support scale-up of manufacturing to support Phase 2 studies and other uses such as expanded access
  – BARDA is also working with manufacturers to offer assistance under the Fill/Finish Network
ZMapp™ – The “Secret Serum”

- ASPR/BARDA awarded a contract to Mapp Biopharmaceutical (San Diego, CA) on September 2 for manufacturing new lots of product
- ZMapp is a combination of 3 monoclonal antibodies that bind to the glycoprotein of Ebola virus (100% Survival NHP 5 dpi)
- ZMapp is manufactured in tobacco plants
- ZMapp has been administered to 6 individuals
  - 2 US Citizens evacuated to US
  - 1 Spanish citizen – 1 dose of 3
  - 3 individuals in Liberia
- BARDA is collaborating with DTRA and NIAID
  - BARDA will perform all manufacturing
  - DTRA – non-clinical study evaluating dose
  - NIAID – IND enabling tox and TXR and potential Phase 1
- BARDA is evaluating alternatives to increase manufacturing capacity, both short- and long-term
  - Additional tobacco plant CMOs
  - Large scale production using cell culture
Additional Therapeutics Under Development

- FDA has, or is, meeting with sponsors to discuss IND enabling studies and potential use of their products

- BioCryst – BCX4430 – adenosine analog
  - Has been evaluated for efficacy in NHP for Marburg
  - Evaluation in NHP for Ebola at USAMRIID

- Tekmira – TKM-Ebola – siRNA
  - Completed Phase 1 SAD, was placed on Clinical hold, revised to partial clinical hold to allow for administration to individuals infected with Ebola
  - Treatment courses sent to Emory, UK, Germany and France

- Medivector – T-705 – RNA polymerase inhibitor
  - Currently in 2, Phase 3 studies for Influenza
  - Being evaluated in NHP for Ebola at USAMRIID
  - Japan has donated 20,000 treatment courses to WHO

- BARDA is currently working with our PHEMCE partners to determine how BARDA can assist in manufacturing and/or development of candidate products
Thank You

- ASPR Leadership
- PHEMCE partners
- BARDA Leadership
- AMCG
- BARDA Team
  - CBRN
  - MFE
  - Regulatory
  - Clinical
  - Influenza
  - DMD
  - SST
  - ADS – Lead for modeling efforts across the USG and with International partners