Ebola Outbreak Response: Testing & Guidance for Clinical Laboratories

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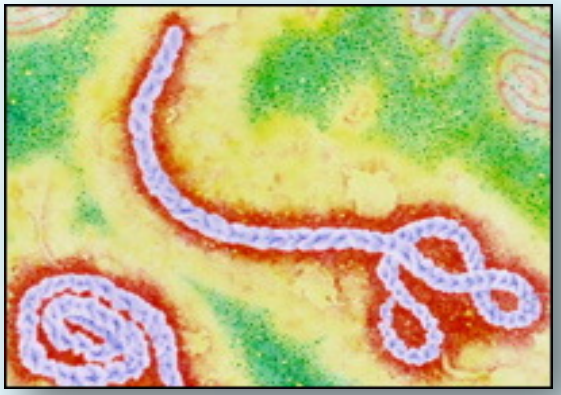
Topics for this Presentation

- Overview of Emergency & Response
- Diagnostics
- Testing at CDC and Laboratory Response Network
- CDC Guidance for Clinical Laboratories
- Problems Identified by CDC Guidance

CDC Ebola Response

Ebola Virus

- Prototype Viral Hemorrhagic Fever Pathogen
  - Filovirus: enveloped, non-segmented, negative-stranded RNA virus
  - Severe disease with high case fatality
  - Absence of specific treatment or vaccine



- Ebola virus outbreaks recognized since 1976
- 2014 West Africa Ebola outbreak caused by *Zaire ebolavirus* species

Ebola Virus Disease – West Africa Outbreak

As of 11/02/2014

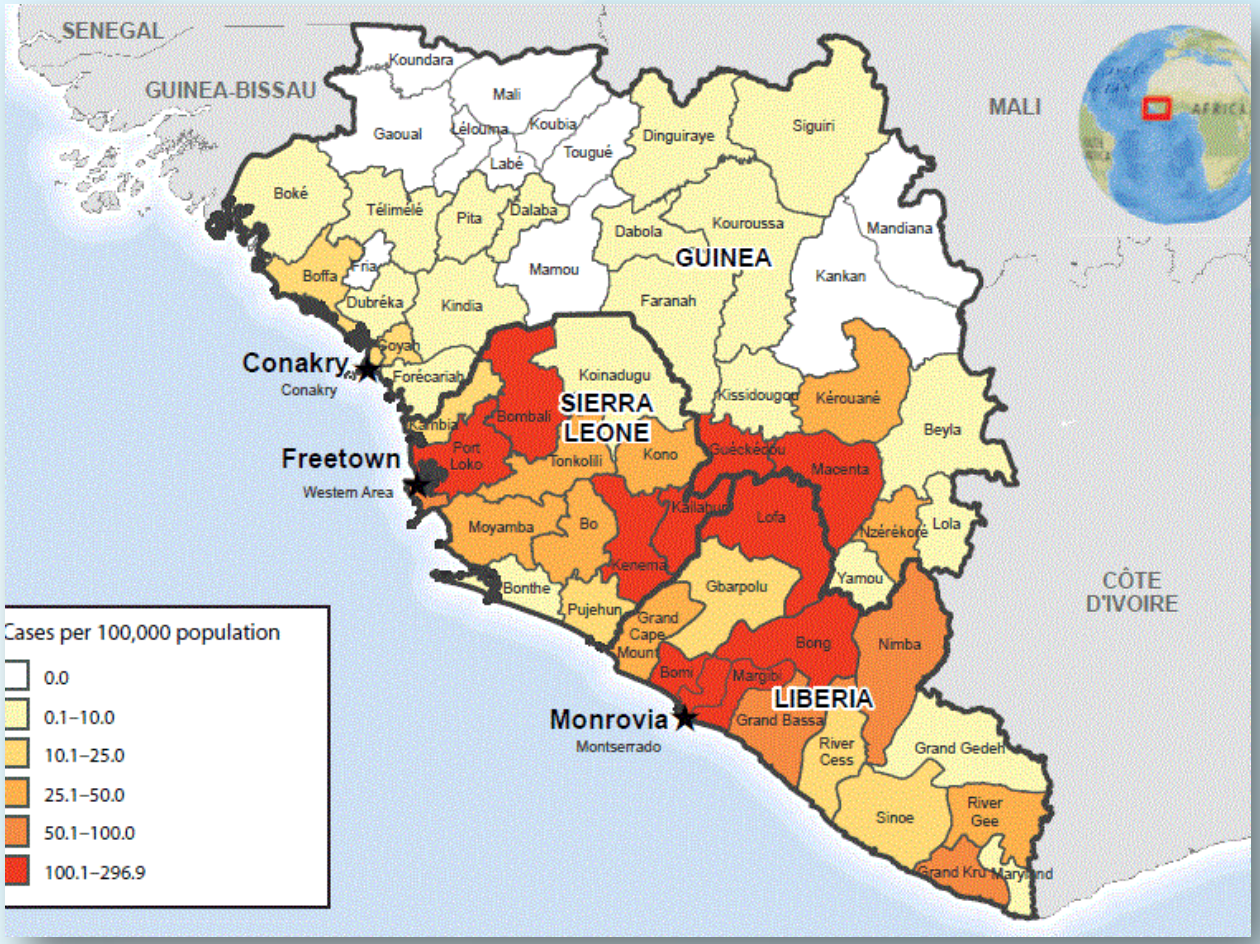
	Reporting Date	Total Cases	Confirmed Cases	Total Deaths
Guinea	10/27/14	1,906	1,391	997
Liberia	10/25/14	6,535	2,515	2,413
Sierra Leone	10/27/14	5,235	3,700	1,500
Nigeria	10/15/14	20	19	8
Spain	10/27/14	1	1	0
Senegal	10/15/14	1	1	0
United States	10/24/14	4	4	1
Mali	10/23/14		1	1
Totals		**13,733**	**7,632**	**4,920**

Updated case counts available at http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/case-counts.html.

*Reported by WHO using data from Ministries of Health

**The outbreaks of EVD in Senegal and Nigeria were declared over on October 17 and 19, respectively.

2014 Ebola Outbreak in West Africa

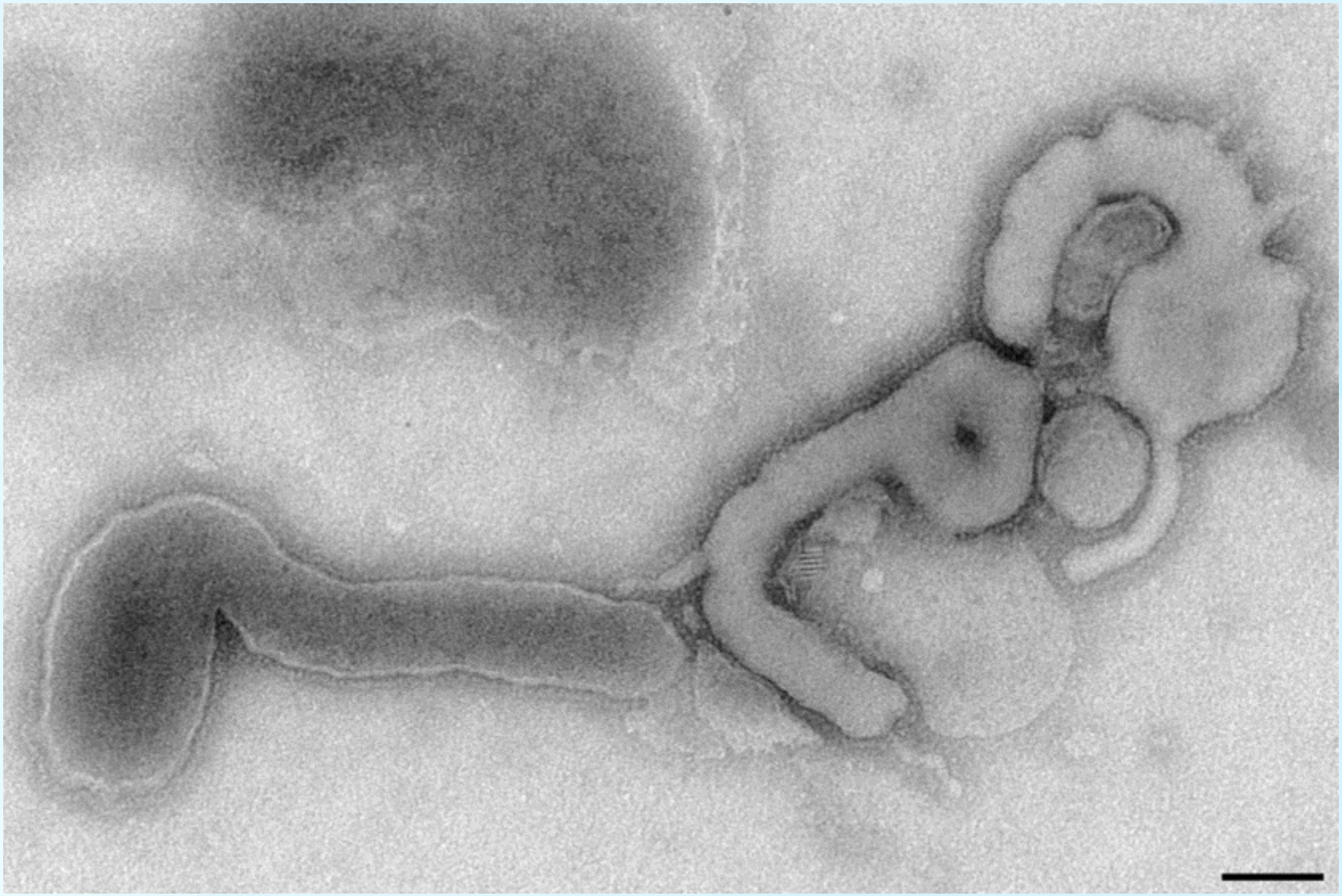


* Cumulative number of reported EVD cases per 100,000 persons since December 22, 2013.
MMWR 2014;63(43):978-981

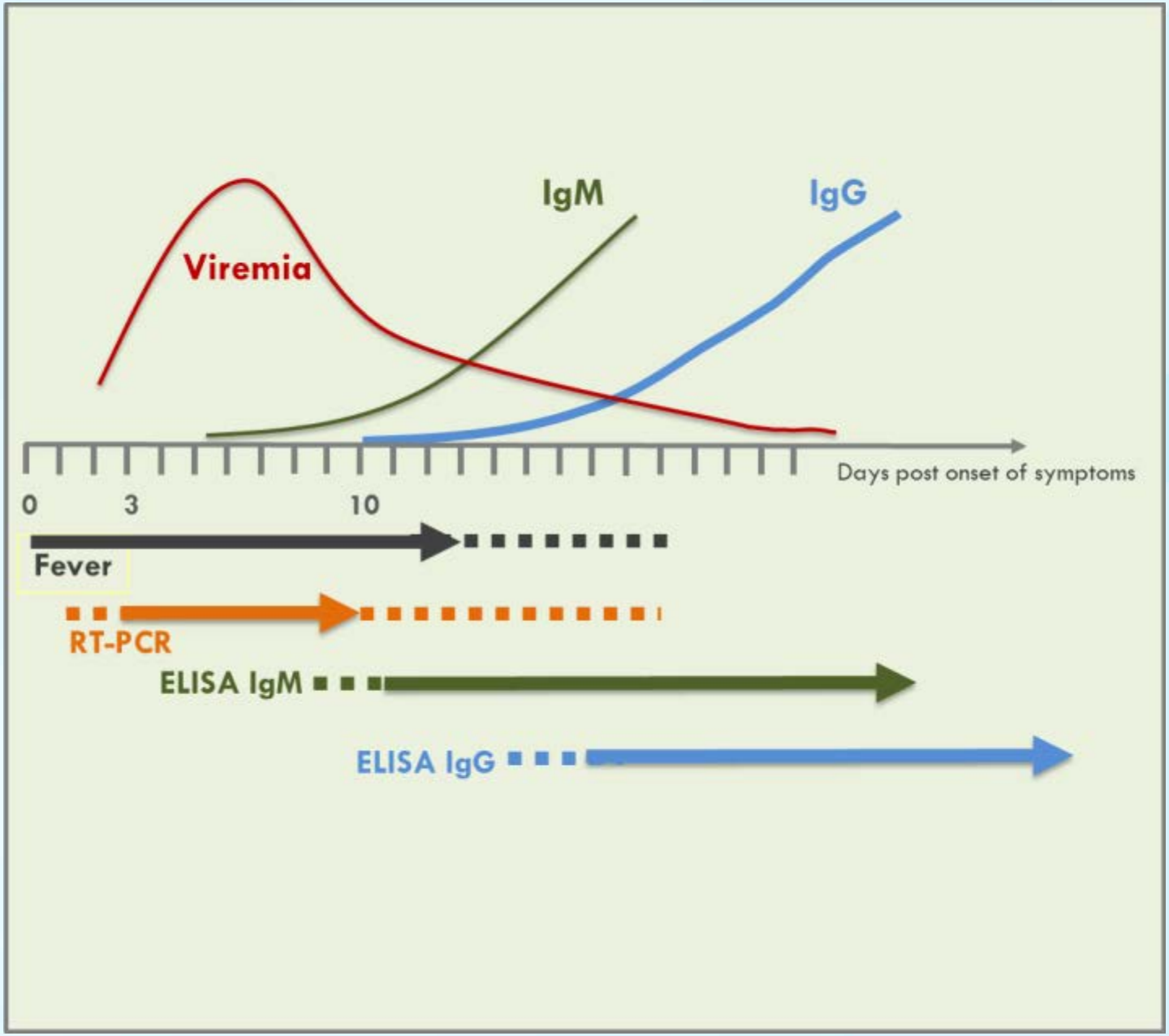
US Ebola Virus Disease Cases

- **Ebola Virus Disease has been diagnosed in four people with onset of disease in the US, as of 11/2/14**
  - **Index patient** – Symptoms developed on September 24, 2014 approximately four days after arrival, sought medical care at Texas Health Presbyterian Hospital of Dallas on September 26, was admitted to hospital on September 28, testing confirmed EVD on September 30, patient died October 8.
  - **TX Healthcare Worker, Case 2** – Cared for index patient, was self-monitoring and presented to hospital reporting low-grade fever, diagnosed with EVD on October 10, recovered and released from NIH Clinical Center October 24.
  - **TX Healthcare Worker, Case 3** – Cared for index patient, was self-monitoring and reported low-grade fever, diagnosed with EVD on October 15, recovered and released from Emory University Hospital in Atlanta October 28.
  - **NY Medical Aid Worker, Case 4** – Worked with Ebola patients in Guinea, was self-monitoring and reported fever, diagnosed with EVD on October 24, currently in isolation at Bellevue Hospital in New York City.

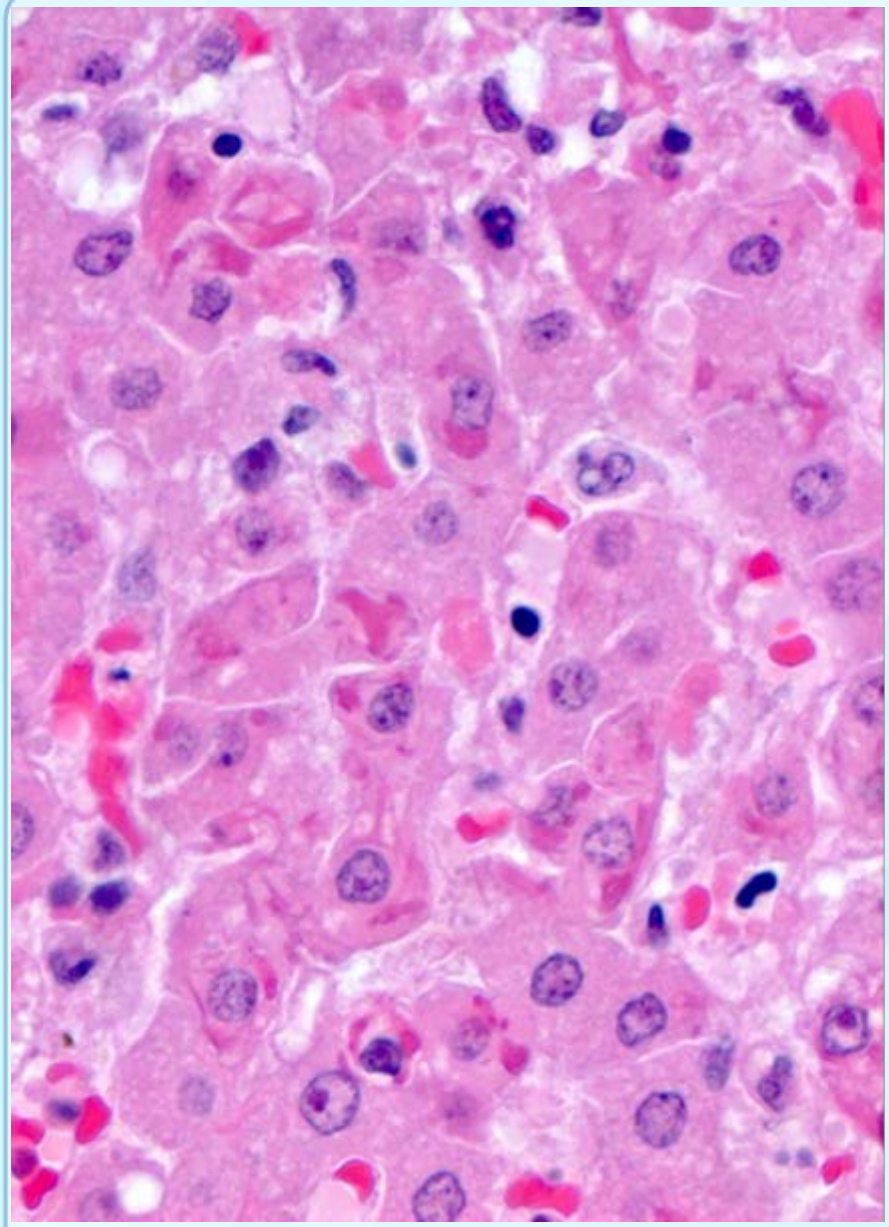
Information on U.S. EVD cases available at http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/united-states-imported-case.html.

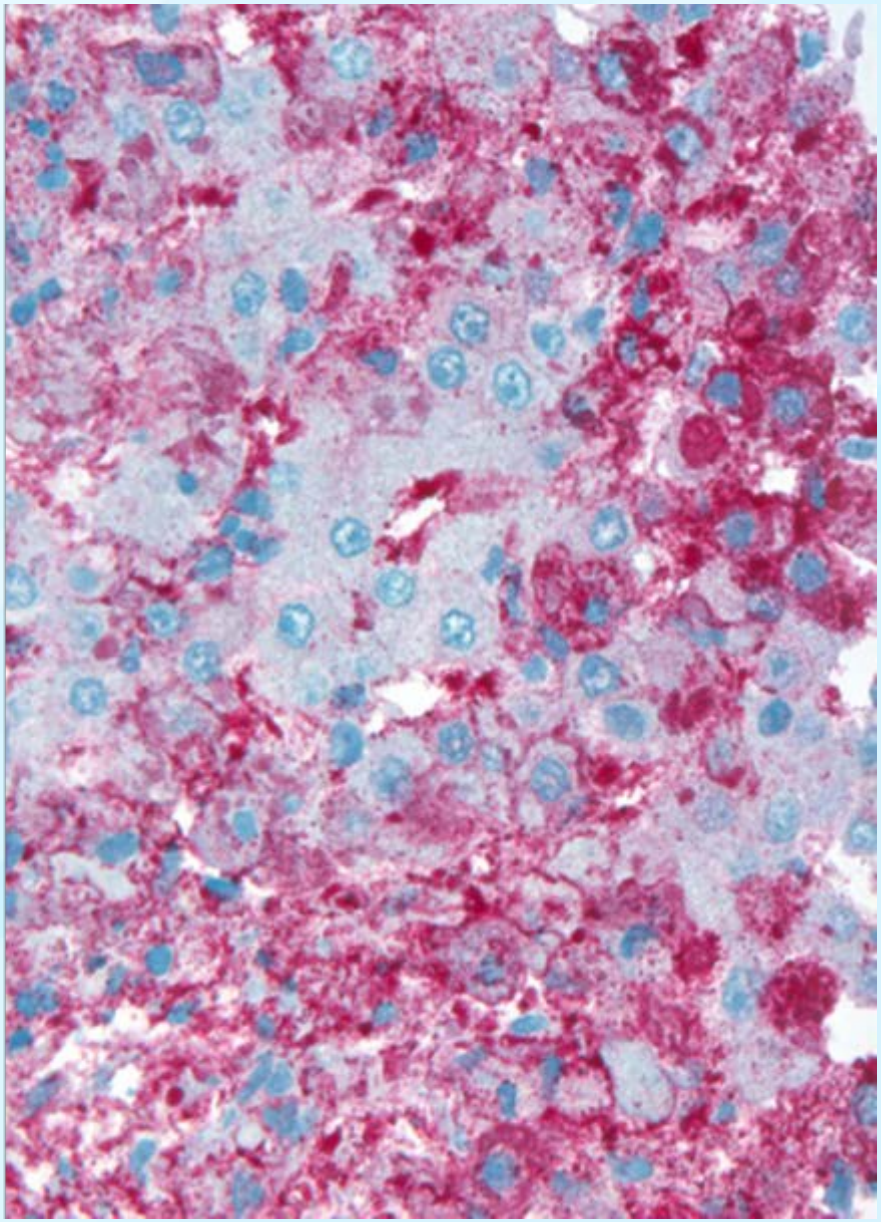


EM courtesy of Maureen G. Metcalfe, Infectious Disease Pathology Branch (IDPB), CDC)



Courtesy of Viral Special Pathogens Branch, CDC





EBOV

Ebola Virus Disease- General Laboratory Findings

- **Early**
  - Thrombocytopenia (50,000–100,000/μL range)
  - Leukopenia
  - Transaminase elevation
- **Later**
  - Electrolyte abnormalities from fluid shifts
  - Coagulation: PT and PTT prolonged
  - Renal: proteinuria, increased creatinine

Ebola Viral Disease Diagnosis

- **Real Time PCR (RT-PCR)**
  - Used to diagnose acute infection
  - More sensitive than antigen detection ELISA
  - Targets specific viral genetic fragments
  - Detects viral DNA present in blood from near onset to resolution
  - Has not been shown to detect disease in asymptomatic or pre-symptomatic individuals

Interpreting Negative Ebola RT-PCR Result

- **If symptoms started ≥3 days before the negative result**
  - EVD is unlikely → consider other diagnoses
  - Infection control precautions for EVD can be discontinued unless clinical suspicion for EVD persists
- **If symptoms started <3 days before the negative RT-PCR result**
  - Interpret result with caution
  - Repeat the test at ≥72 hours after onset of symptoms
  - Keep in isolation as a suspected case until a repeat RT-PCR ≥72 hours after onset of symptoms is negative

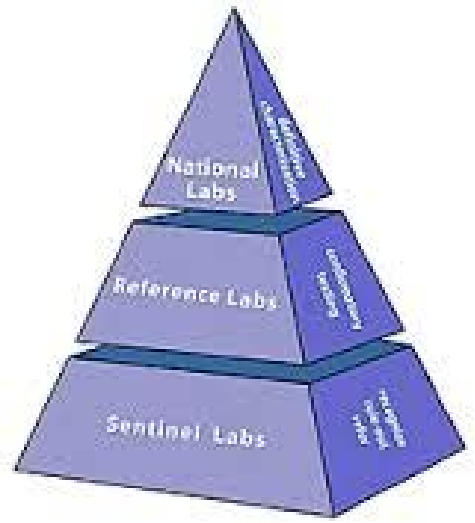
FDA Emergency-Use-Authorized Ebola Diagnostics

Date of Initial EUA	Assay	Analytic Time	Current Role in US Ebola Response	US Locations
08/05/14	DoD EZ1 real-time RT-PCR	4-6 hours	Negative Test Can Rule Out; Positive Test Requires Confirmation	LRN labs (currently about 30)
10/10/14	CDC Ebola Virus NP real-time RT-PCR	4-6 hours	Confirmatory test when combined with test below	CDC
10/10/14	CDC Ebola Virus VP40 real-time RT-PCR	4-6 hours	Confirmatory test when combined with test above	CDC
10/25/14	BioFire Defense FilmArray Biothreat E test	1 hour	Rapid evaluation at facilities; Negatives & positives currently require retesting at LRN or CDC.	Hospital and other laboratories

Information current as of 11/02/14

Laboratory Response Network

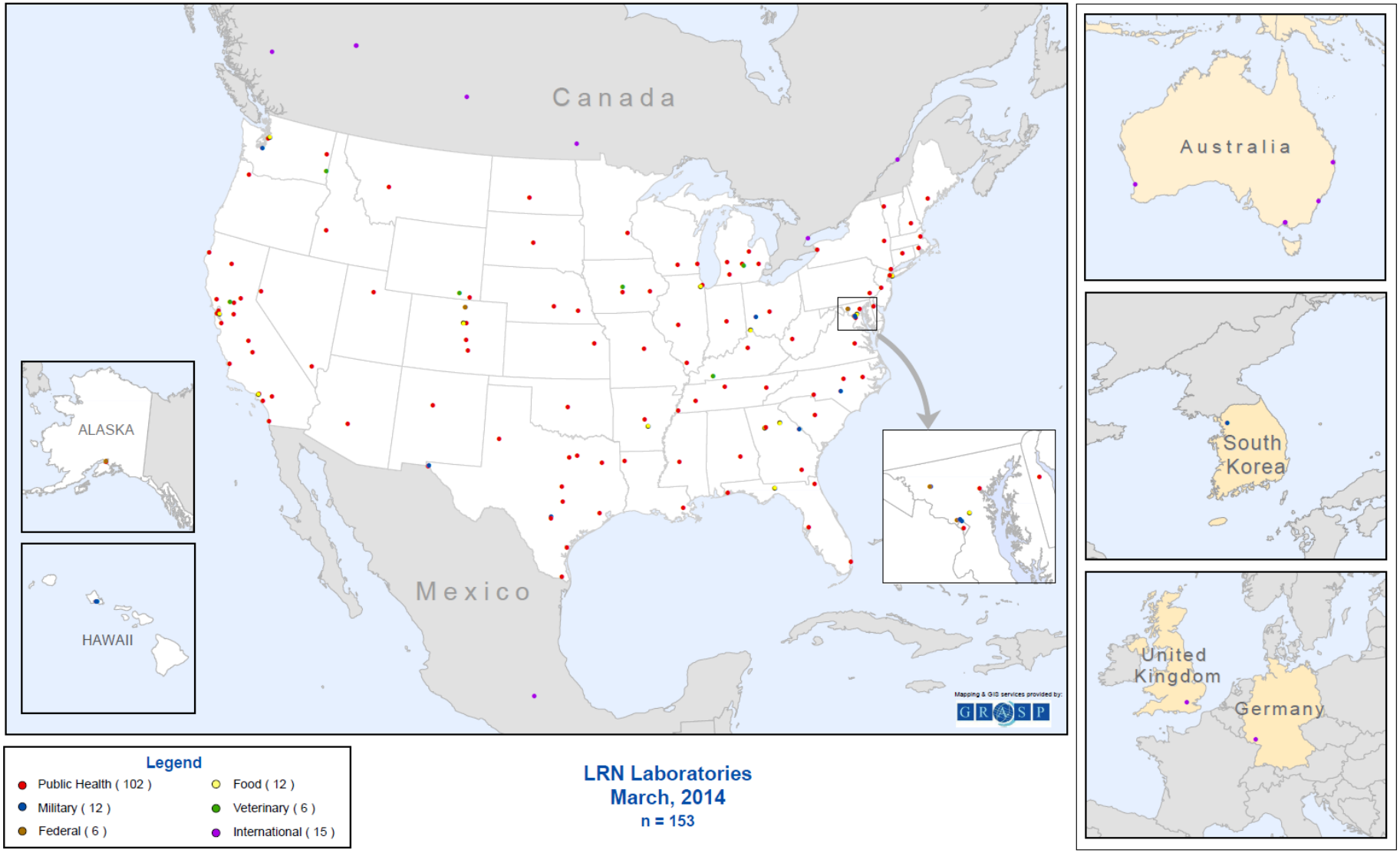
LRN™
LABORATORY RESPONSE NETWORK



- Network of laboratories
- Common policies, procedures and protocols
- Detection, characterization, & response to biological & chemical agents, including emerging infectious diseases
- High confidence results to inform high consequence public health decisions
- Clinical (chem & bio) and environmental samples (bio)

National Center for Emerging Zoonotic and Infectious Diseases
Division of Preparedness and Emerging Infections

Laboratory Preparedness and Response Branch



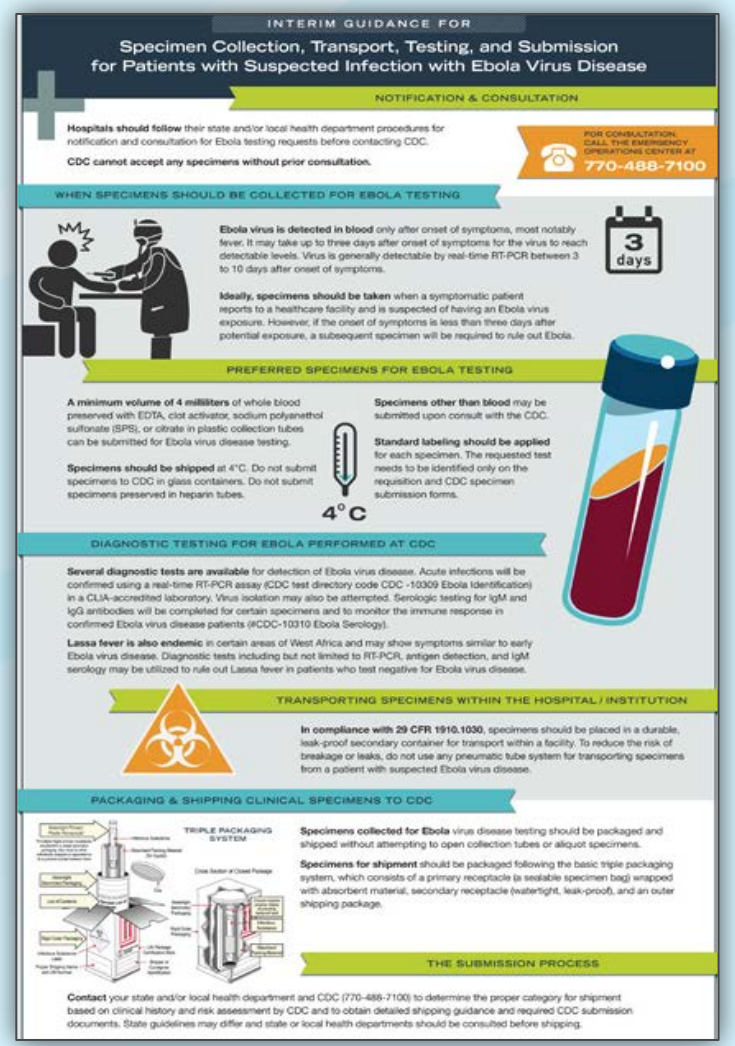
Legend

- Public Health (102)
- Military (12)
- Federal (6)
- Food (12)
- Veterinary (6)
- International (15)

LRN Laboratories
March, 2014
n = 153

How to Get Ebola Tests from Public Health Laboratories

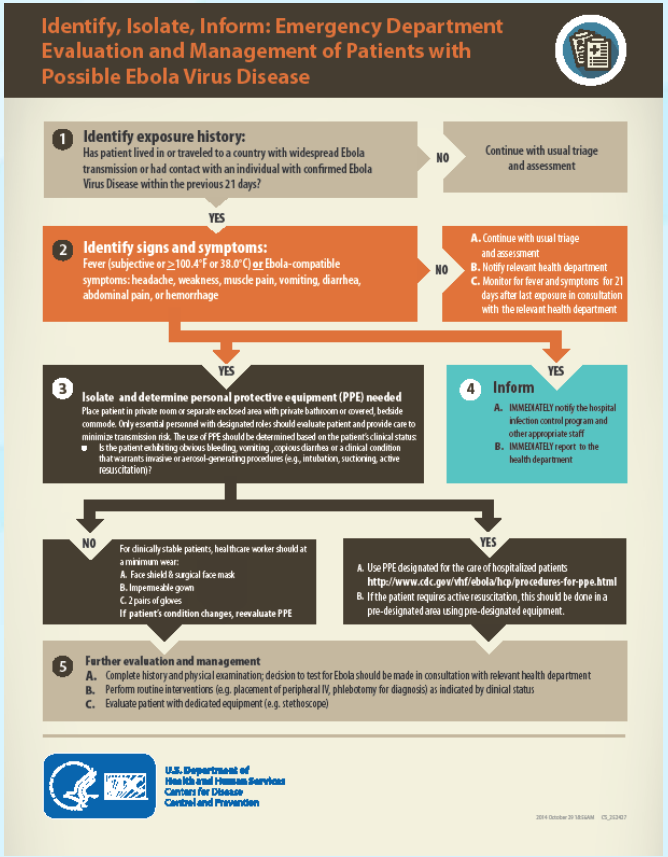
- CDC has developed interim guidance for U.S. laboratory workers and other healthcare personnel who collect or handle specimens
- This guidance includes information about the appropriate steps for collecting, transporting, and testing specimens from patients who are suspected to be infected with Ebola
- Specimens should NOT be shipped to LRN or CDC without consultation with local/state health departments and CDC.



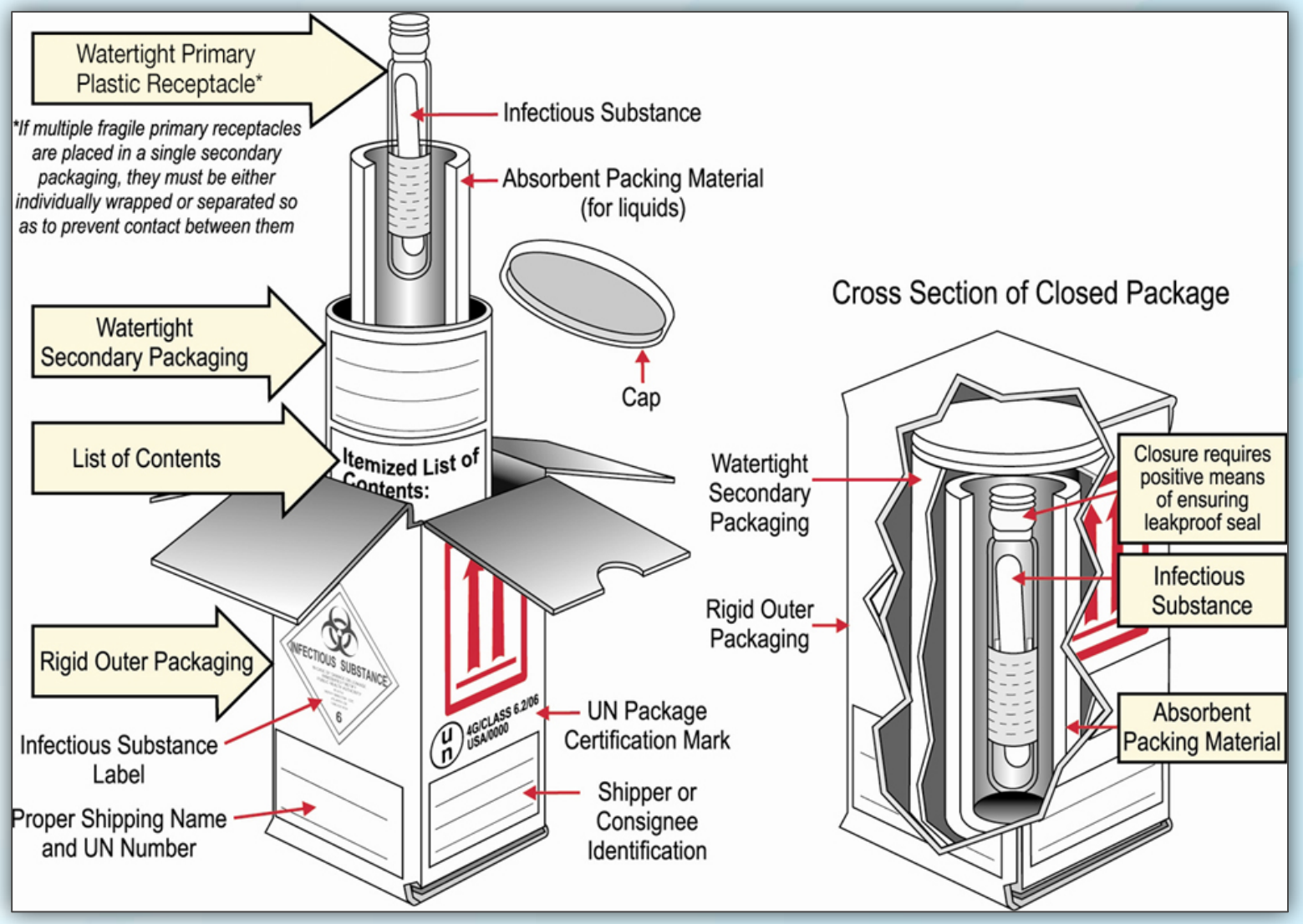
Information available at: http://www.cdc.gov/vhf/ebola/hcp/interim-guidance-specimen-collection-submission-patients-suspected-infection-ebola.html

Current CDC Guidance for Specimen Collection from a Person Under Investigation for Ebola

- **Identify, Isolate & Inform before collecting a specimen for Ebola testing.**
- Recommended personal protective equipment based on clinical presentation. If patient is "dry:"
  - 2 pairs of gloves
  - Water resistant gown
  - Full face shield & surgical mask



Packaging & Shipping Clinical Specimens to CDC for Ebola Testing



http://www.cdc.gov/vhf/ebola/hcp/packaging-diagram.html

CDC Guidance for Routine Testing of Persons Under Investigation in Clinical Laboratories

- Follow OSHA bloodborne pathogens standard. Employer responsibilities in clinical lab:
  - Provide written updated exposure control plan
  - Consider all body fluids as potentially infectious
  - Institute hierarchy of engineering controls, work practice controls, personal protective equipment

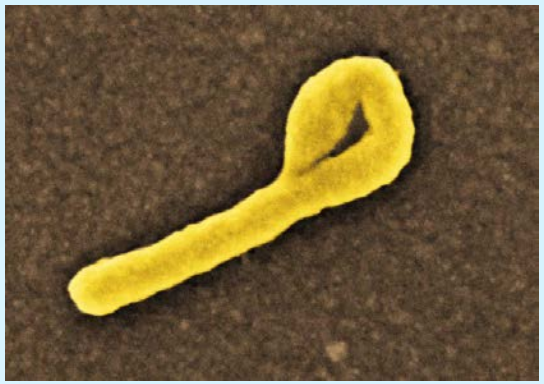
CDC Guidance for Routine Testing of Persons Under Investigation in Clinical Laboratories

- Responsible authority should conduct risk assessment:
  - Determine potential for sprays, splashes, or aerosols
  - Adjust engineering controls, work practices, or personal protective equipment to protect skin, eyes, mucous membranes

Problems Identified with Routine Testing of Persons Under Investigation in Clinical Laboratories

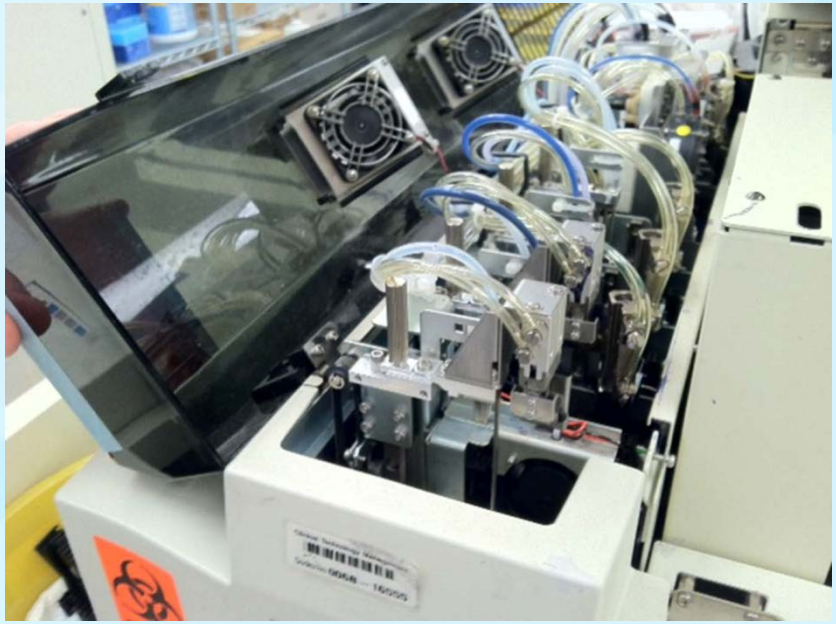
- Ebola is very scary
- Ebola has very low infectious dose
- Ebola has very high morbidity & mortality
- Lack of data on safety of routine clinical laboratory procedures for Ebola specimens

- Ebola long considered BSL-4 agent
- CDC works with Ebola in BSL-4 (In US)
- General clinical laboratory is BSL-2



Problems Identified with Routine Testing of Persons Under Investigation in Clinical Laboratories

- Lack of data on decontamination of laboratory instruments, specifically for Ebola



Problems Identified with Routine Testing of Persons Under Investigation in Clinical Laboratories

- No organization evaluates, monitors, or approves clinical laboratory instruments for blood-borne pathogen safety

- Some instrument manufacturers have informed users that testing Ebola specimens would void warranties or prevent reuse of the instrument

Problems Identified with Routine Testing of Persons Under Investigation in Clinical Laboratories

- Emory and Nebraska did NOT perform testing of Ebola patients in their regular clinical laboratories

- Some professional organizations have recommended that laboratories limit testing on persons under investigation for Ebola patients in their regular clinical laboratories

Problems Identified with Routine Testing of Persons Under Investigation in Clinical Laboratories

- Some national reference laboratories have requested that clients not submit specimens from persons under investigation for Ebola

From a reference laboratory:

"Ebola Specimen Guidelines
Ebola virus disease, one of numerous viral hemorrhagic fevers, is a severe, often fatal disease in humans and nonhuman primates. Any laboratory testing requested on specimens from suspected Ebola patients should **not** be sent to …… but held until results for Ebola testing are confirmed as negative by the CDC."

Ebola:
Current Approach to Care in the US

- **Persons Under Investigation:**
  - Individuals entering the US from outbreak countries are now being actively monitored for symptoms
  - As soon as symptoms develop they are directed to an appropriate hospital emergency department for evaluation
- **Persons with Ebola:**
  - Individuals with Ebola will be cared for in facilities that self-identified and been evaluated for preparedness to care for Ebola patients

Long Term Issues for Clinical Laboratories

- How to assure the safety of laboratory instruments?
- How to assure that clinical laboratories are prepared for biological threats and emerging infections diseases?
- How to assure compliance with standard laboratory precautions and the OSHA bloodborne standard?
- Who inspects laboratories for safety?

Discussion

For more information please contact Centers for Disease Control and Prevention

1600 Clifton Road NE, Atlanta, GA 30333
Telephone: 1-800-CDC-INFO (232-4636)/TTY: 1-888-232-6348
Visit: www.cdc.gov | Contact CDC at: 1-800-CDC-INFO or www.cdc.gov/info