

# **Ebola Outbreak Response: Testing & Guidance for Clinical Laboratories**

**Toby L Merlin, MD.**

Director, Division of Preparedness and Emerging Infections

Clinical Laboratory Improvement Advisory Committee

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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

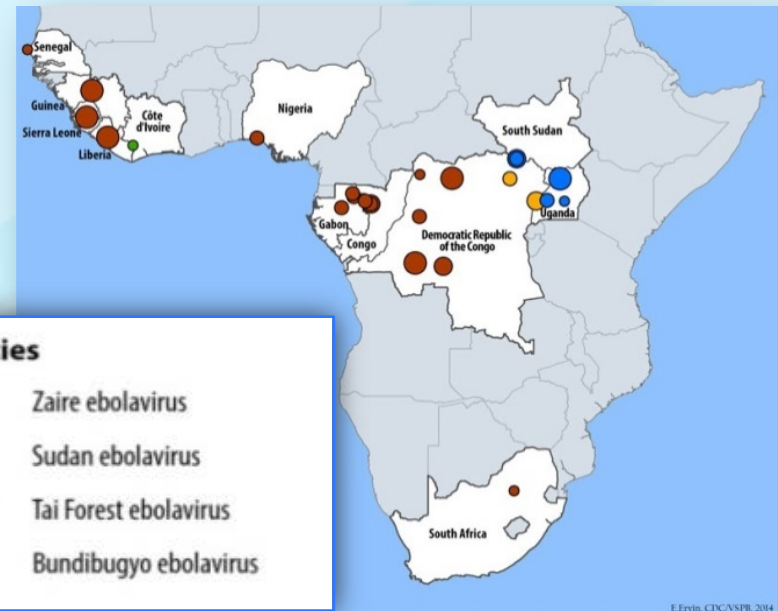


# Ebola Virus

- 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

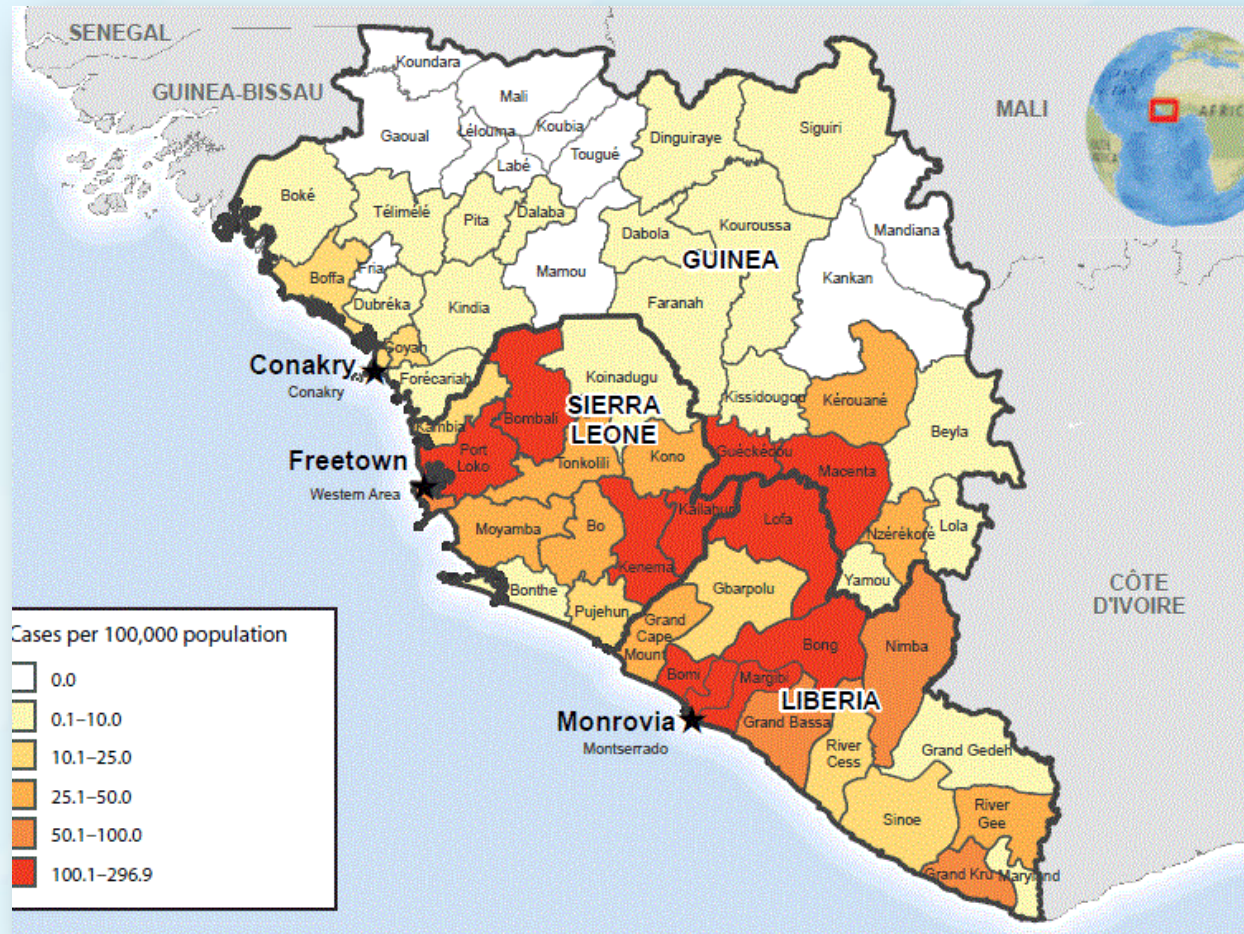
	Reporting Date	Total Cases	Confirmed Cases	Total Deaths
Guinea	10/27/14	1,906	1,391	997
Liberia	10/25/14	6,535	2,515	2,413
Sierra Leone	10/27/14	5,235	3,700	1,500
Nigeria	10/15/14	20	19	8
Spain	10/27/14	1	1	0
Senegal	10/15/14	1	1	0
United States	10/24/14	4	4	1
Mali	10/23/14		1	1
<b>Totals</b>		<b>13,733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

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



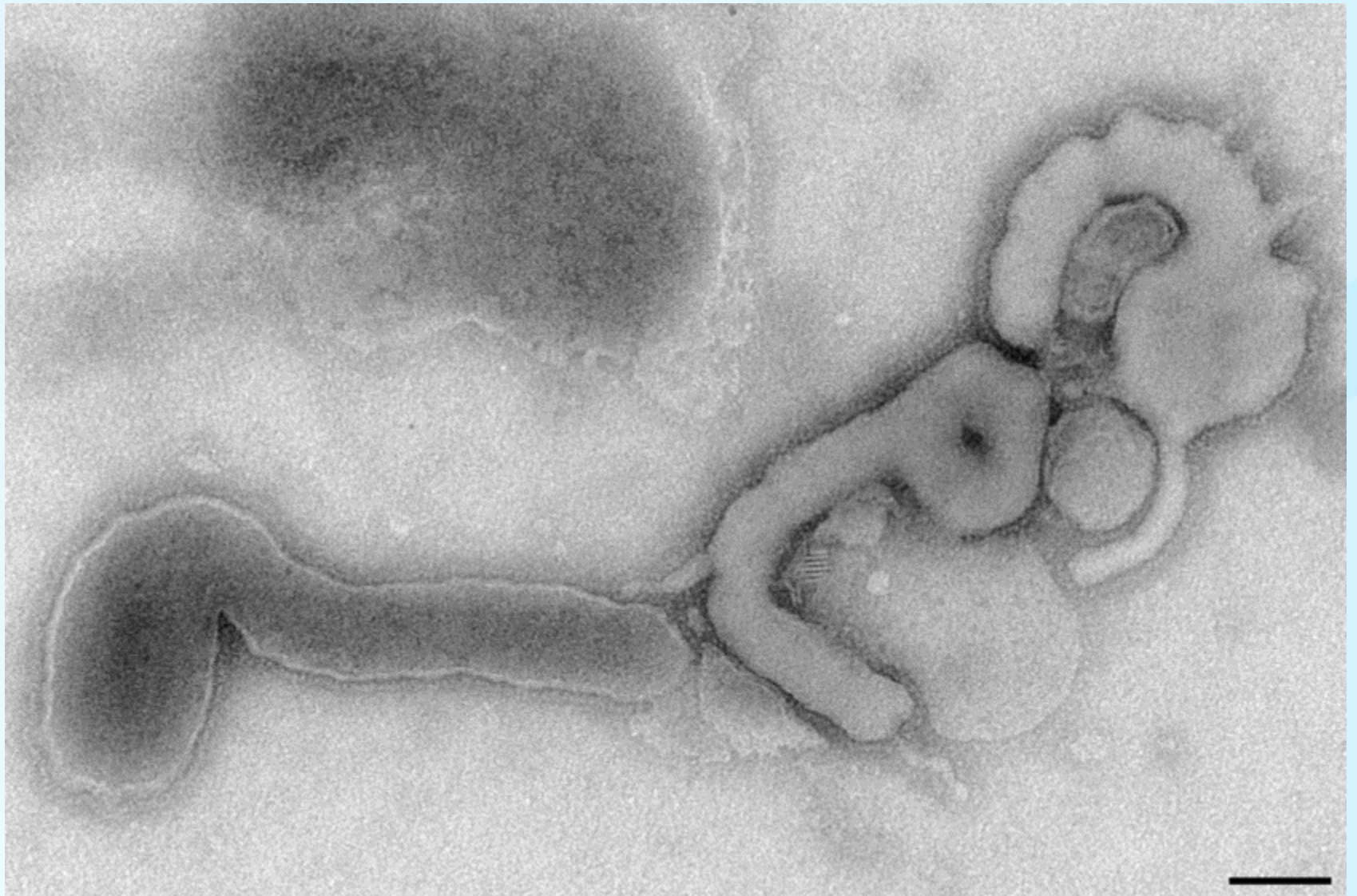
\* Cumulative number of reported EVD cases per 100,000 persons since December 22, 2013.

[MMWR 2014;63\(43\):978-981](#)

# US Ebola Virus Disease Cases

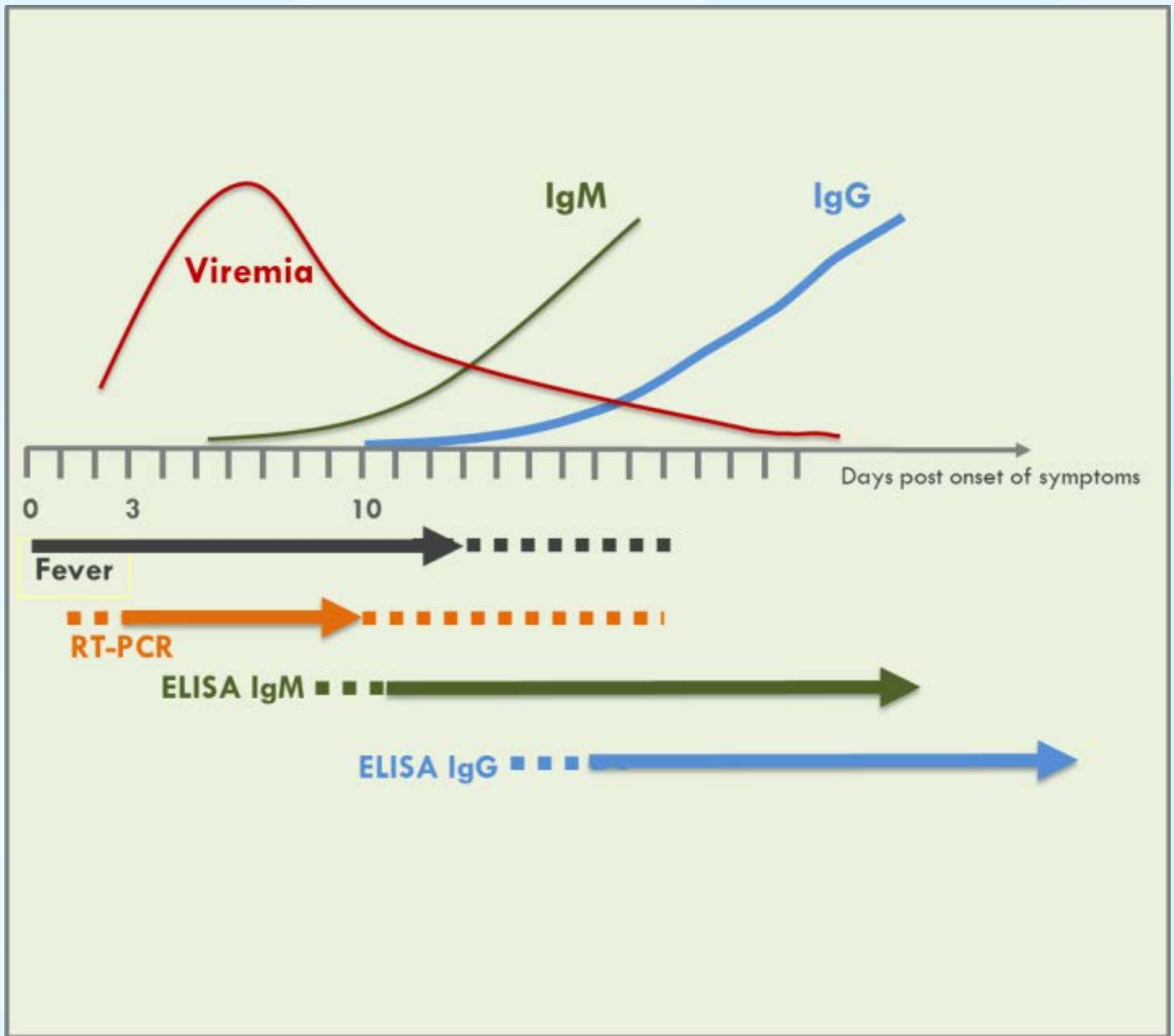
- **Ebola Virus Disease has been diagnosed in four people with onset of disease in the US, as of 11/2/14**
  - **Index patient** – Symptoms developed on September 24, 2014 approximately four days after arrival, sought medical care at Texas Health Presbyterian Hospital of Dallas on September 26, was admitted 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.

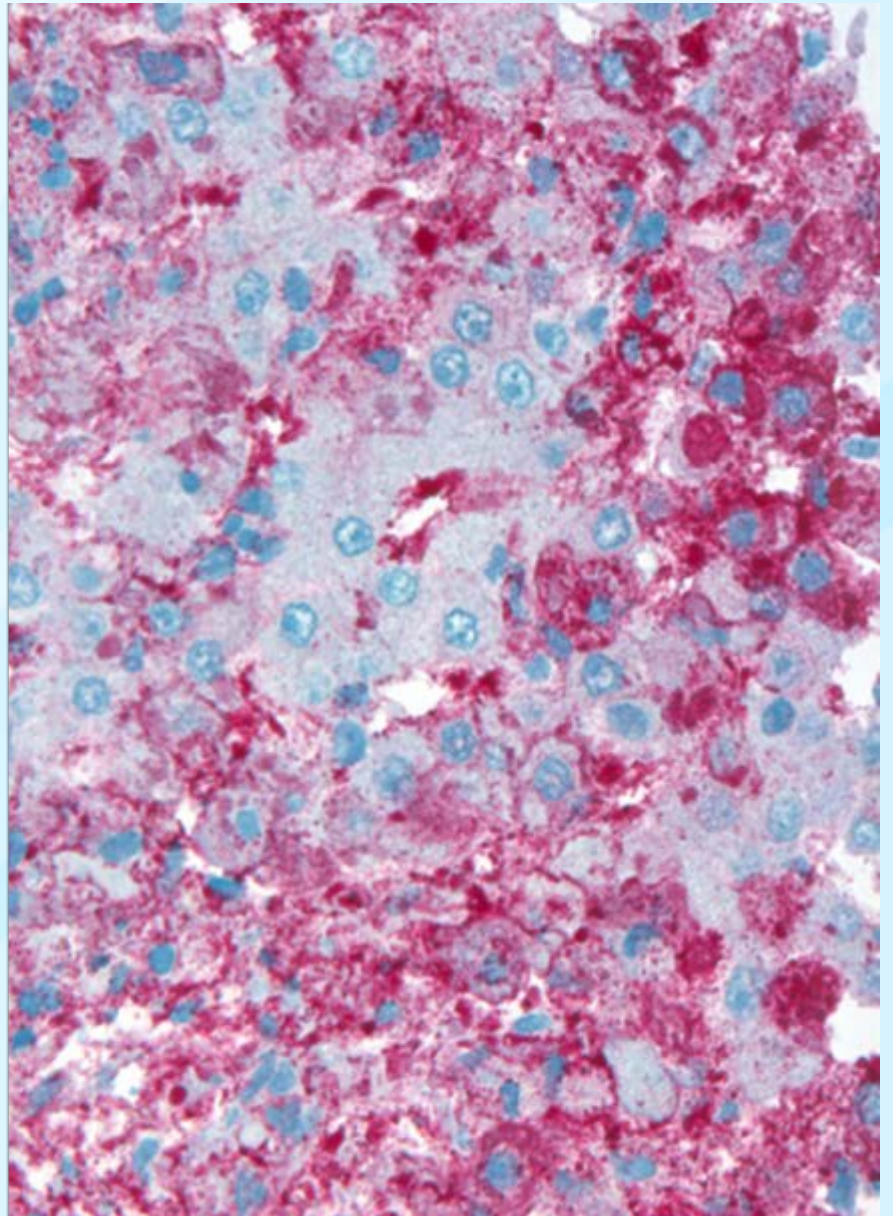
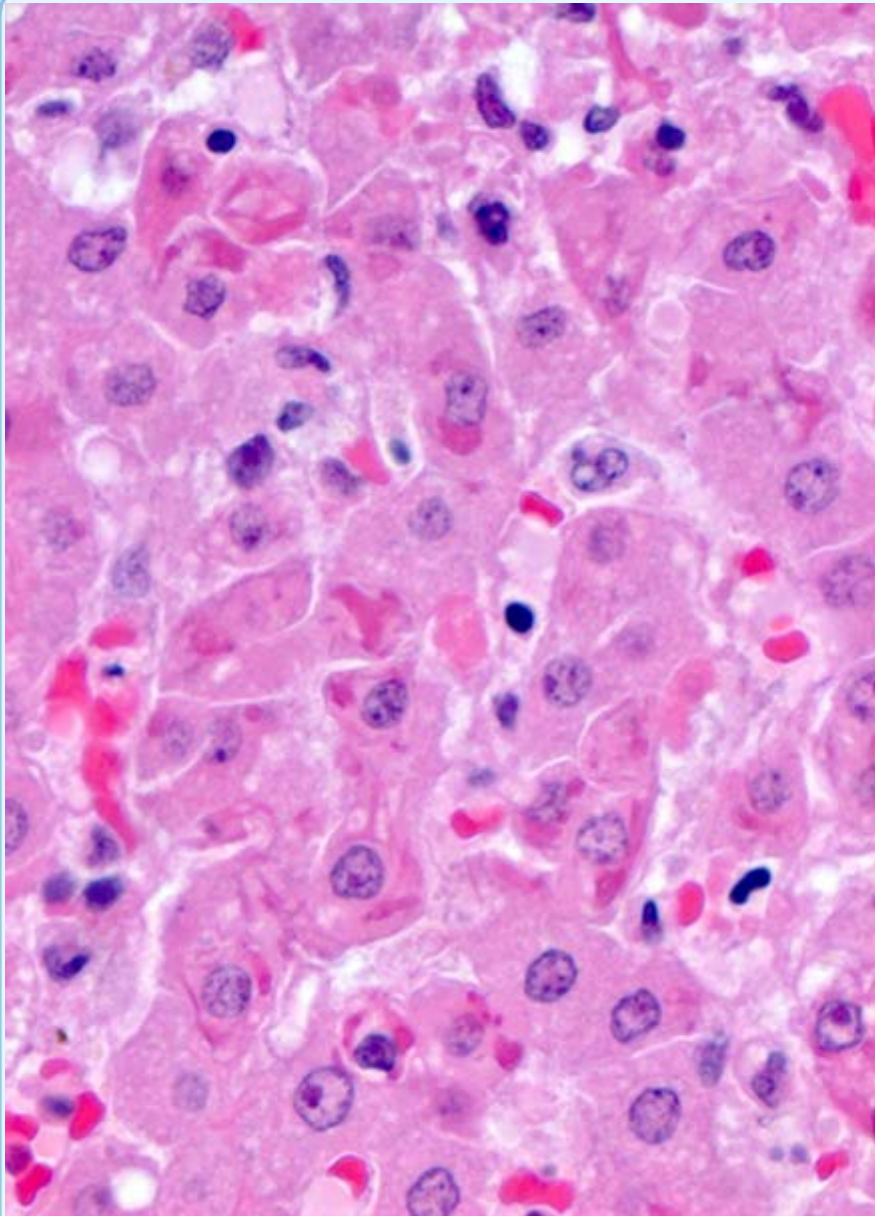
Information on U.S. EVD cases available at <http://www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/united-states-imported-case.html>.



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







# Ebola Virus Disease- General Laboratory Findings

## ▪ Early

- Thrombocytopenia (50,000–100,000/ $\mu$ L 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

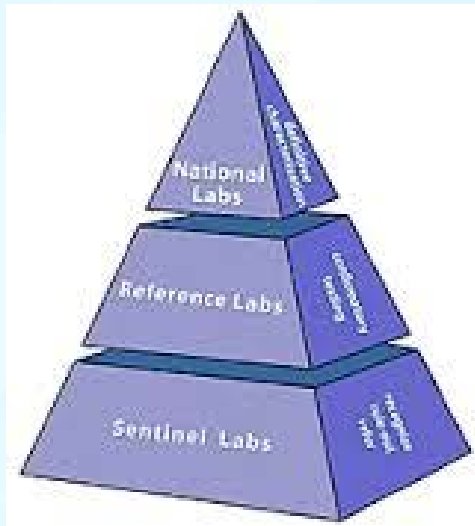
## Interpreting Negative Ebola RT-PCR Result

- **If symptoms started  $\geq 3$  days before the negative result**
  - EVD is unlikely  $\rightarrow$  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  $\geq 72$  hours after onset of symptoms
  - Keep in isolation as a suspected case until a repeat RT-PCR  $\geq 72$  hours after onset of symptoms is negative

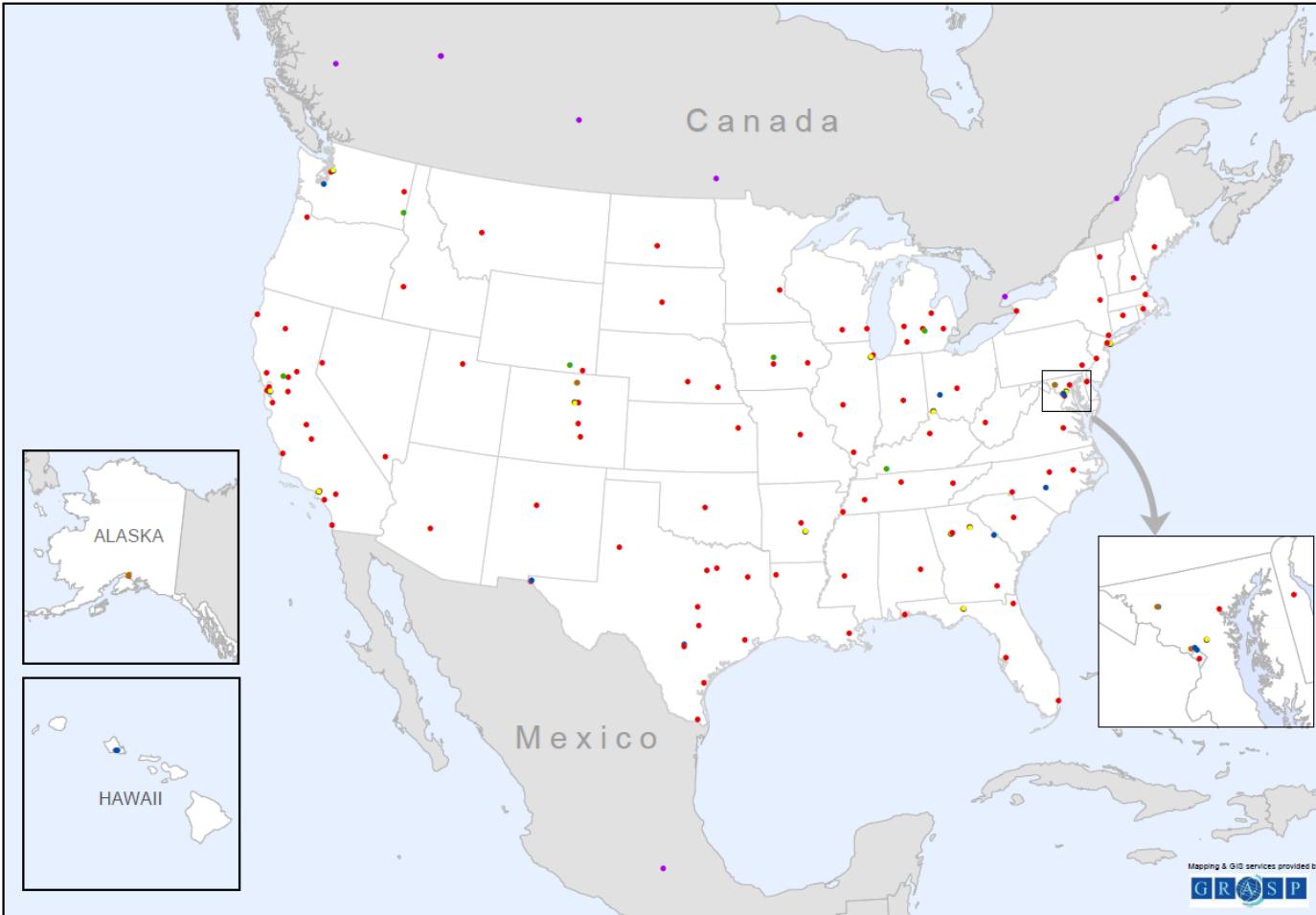
# FDA Emergency-Use-Authorized Ebola Diagnostics

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

# 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)



**Legend**

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

**LRN Laboratories**  
 March, 2014  
 n = 153

Mapping & GIS services provided by:  




# 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.

**INTERIM GUIDANCE FOR Specimen Collection, Transport, Testing, and Submission for Patients with Suspected Infection with Ebola Virus Disease**

**NOTIFICATION & CONSULTATION**

Hospitals should follow their state and/or local health department procedures for notification and consultation for Ebola testing requests before contacting CDC. CDC cannot accept any specimens without prior consultation.

FOR CONSULTATION, CALL THE EMERGENCY OPERATIONS CENTER AT 770-488-7100

**WHEN SPECIMENS SHOULD BE COLLECTED FOR EBOLA TESTING**

Ebola virus is detected in blood only after onset of symptoms, most notably fever. It may take up to three days after onset of symptoms for the virus to reach detectable levels. Virus is generally detectable by real-time RT-PCR between 3 to 10 days after onset of symptoms.

Ideally, specimens should be taken when a symptomatic patient reports to a healthcare facility and is suspected of having an Ebola virus exposure. However, if the onset of symptoms is less than three days after potential exposure, a subsequent specimen will be required to rule out Ebola.

**PREFERRED SPECIMENS FOR EBOLA TESTING**

A minimum volume of 4 milliliters of whole blood preserved with EDTA, clot activator, sodium polyanethanol sulfonate (SPS), or citrate in plastic collection tubes can be submitted for Ebola virus disease testing.

Specimens should be shipped at 4°C. Do not submit specimens to CDC in glass containers. Do not submit specimens preserved in heparin tubes.

Specimens other than blood may be submitted upon consult with the CDC.

Standard labeling should be applied for each specimen. The requested test needs to be identified only on the requisition and CDC specimen submission forms.

**DIAGNOSTIC TESTING FOR EBOLA PERFORMED AT CDC**

Several diagnostic tests are available for detection of Ebola virus disease. Acute infections will be confirmed using a real-time RT-PCR assay (CDC test directory code CDC-10309 Ebola Identification) in a CLIA-accredited laboratory. Virus isolation may also be attempted. Serologic testing for IgM and IgG antibodies will be completed for certain specimens and to monitor the immune response in confirmed Ebola virus disease patients (CDC-10310 Ebola Serology).

Lassa fever is also endemic in certain areas of West Africa and may show symptoms similar to early Ebola virus disease. Diagnostic tests including but not limited to RT-PCR, antigen detection, and IgM serology may be utilized to rule out Lassa fever in patients who test negative for Ebola virus disease.

**TRANSPORTING SPECIMENS WITHIN THE HOSPITAL / INSTITUTION**

In compliance with 29 CFR 1910.1030, specimens should be placed in a durable, leak-proof secondary container for transport within a facility, to reduce the risk of breakage or leaks. Do not use any pneumatic tube system for transporting specimens from a patient with suspected Ebola virus disease.

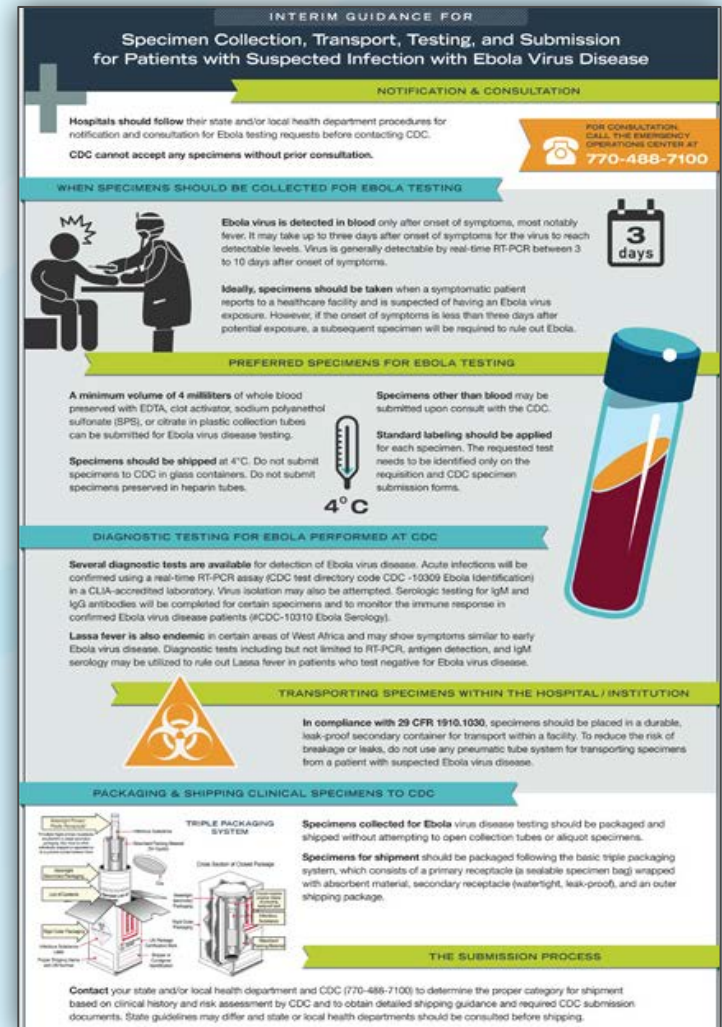
**PACKAGING & SHIPPING CLINICAL SPECIMENS TO CDC**

Specimens collected for Ebola virus disease testing should be packaged and shipped without attempting to open collection tubes or aliquot specimens.

Specimens for shipment should be packaged following the basic triple packaging system, which consists of a primary receptacle (a sealable specimen bag) wrapped with absorbent material, secondary receptacle (watertight, leak-proof), and an outer shipping package.

**THE SUBMISSION PROCESS**

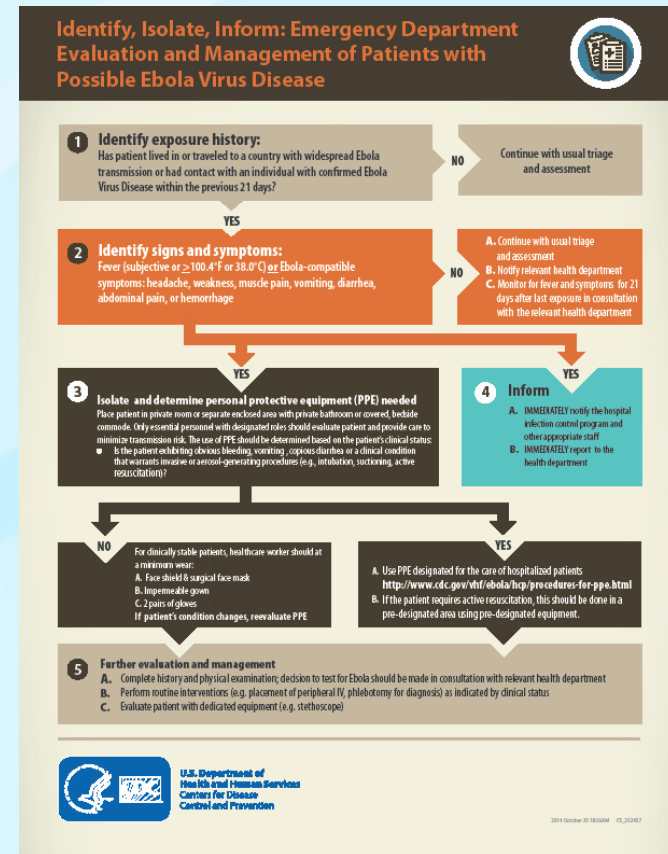
Contact your state and/or local health department and CDC (770-488-7100) to determine the proper category for shipment based on clinical history and risk assessment by CDC and to obtain detailed shipping guidance and required CDC submission documents. State guidelines may differ and state or local health departments should be consulted before shipping.



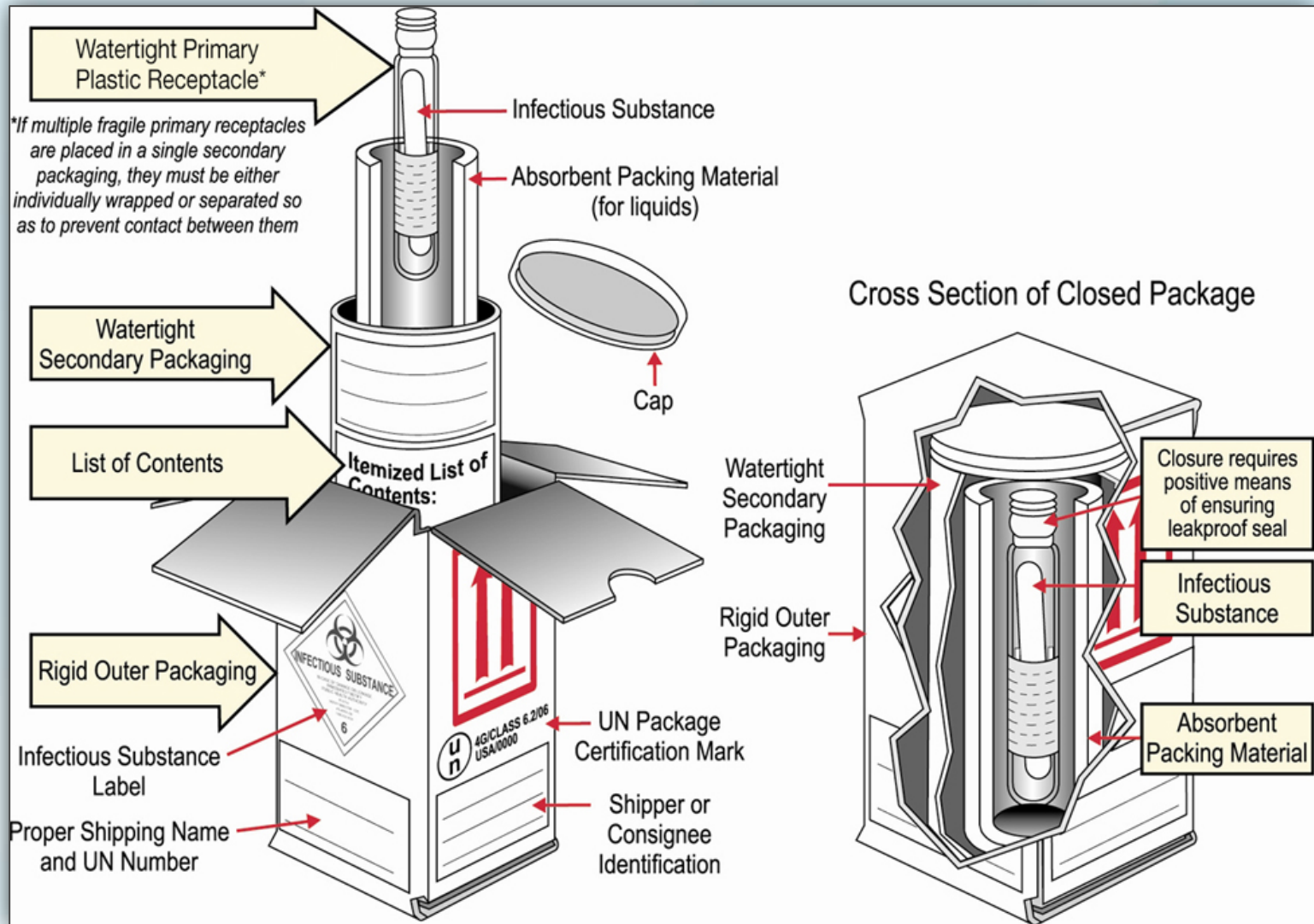
Information available at: <http://www.cdc.gov/vhf/ebola/hcp/interim-guidance-specimen-collection-submission-patients-suspected-infection-ebola.html>

# 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



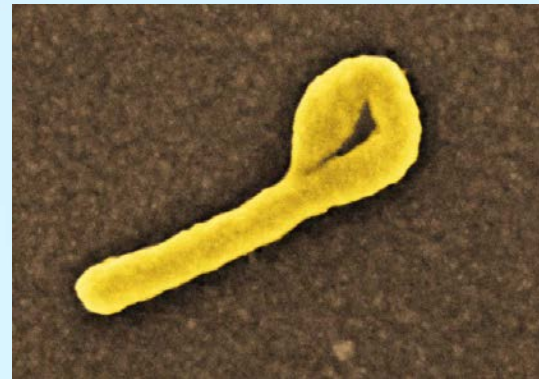
# CDC Guidance for Routine Testing of Persons Under Investigation in Clinical Laboratories

- ❑ 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



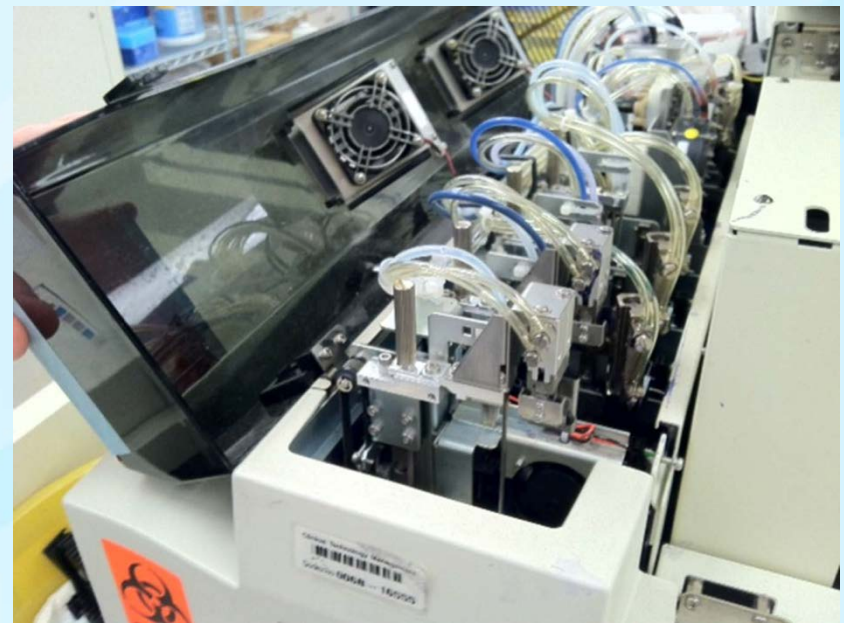
## Problems Identified with Routine Testing of Persons Under Investigation in Clinical Laboratories

- 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](http://www.cdc.gov) | Contact CDC at: 1-800-CDC-INFO or [www.cdc.gov/info](http://www.cdc.gov/info)

The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

