Select Agents in Public Health
Preparedness, Detection, and Response to High-Consequence Pathogens

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Disclaimers

- While some products will be mentioned by name, this is not an endorsement for any product of manufacturer.

- I have no financial conflicts of interest related to this work.

Bioterrorism

bi·o·ter·ror·ism

The intentional release or dissemination of biological agents to kill or incapacitate people, animals, or crops.

Bioterrorism Throughout History

In one of the earliest recorded instances of bioterrorism was in the 6th century BC, Persian armies poisoned wells with a fungus that affects rye plants (*rye ergot*).

Ergotism or *St. Anthony's fire* causes burning sensation, muscle spasms, fever, hallucinations, and in severe cases gangrene and death.

Saint Anthony Tormented by Demons (1512–1516)
Matthias Grunewald

Claviceps sp.

Examples of Biological Warfare

Year	Event
1155	Emperor Barbarossa poisons water wells with human bodies, Tortona, Italy
1346	Mongols catapult bodies of plague victims over the city walls of Caffa, Crimean Peninsula
1495	Spanish mix wine with blood of leprosy patients to sell to their French foes, Naples, Italy
1650	Polish fire saliva from rabid dogs towards their enemies
1675	First deal between German and French forces not to use 'poison bullets'
1763	British distribute blankets from smallpox patients to native Americans
1797	Napoleon floods the plains around Mantua, Italy, to enhance the spread of malaria
1863	Confederates sell clothing from yellow fever and smallpox patients to Union troops, USA

Frischknect. The History of biological warfare. EMBO Rep. 2003

Bioweapons Research

A disturbing example was Japan's notorious bioweapons program, which conducted research on military and civilian prisoners before and during WWII. These experiments involved infecting prisoners with often fatal inocula of *F. tularensis* and other pathogens to study disease effects and pathophysiology

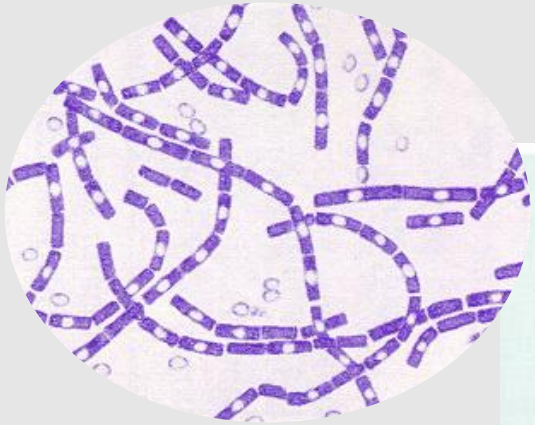
The Biological Weapons Convention

Global, multilateral disarmament treaty signed in 1975

Prohibits the development, production, stockpiling, acquisition, retention or transfer of bioweapons

Bioweapon Manufacture

- In 1979, a sudden increase in human and animal cases of Anthrax was reported in the USSR.
- The USSR claimed it was from consumption of contaminated meat.
- It was later discovered a HEPA filter for air leaving the facility was taken off overnight for repairs.
- At least 66 people died, many more illness in 6 different villages. Most of this is farm land so many animal deaths more than 50 miles downwind from the facility.

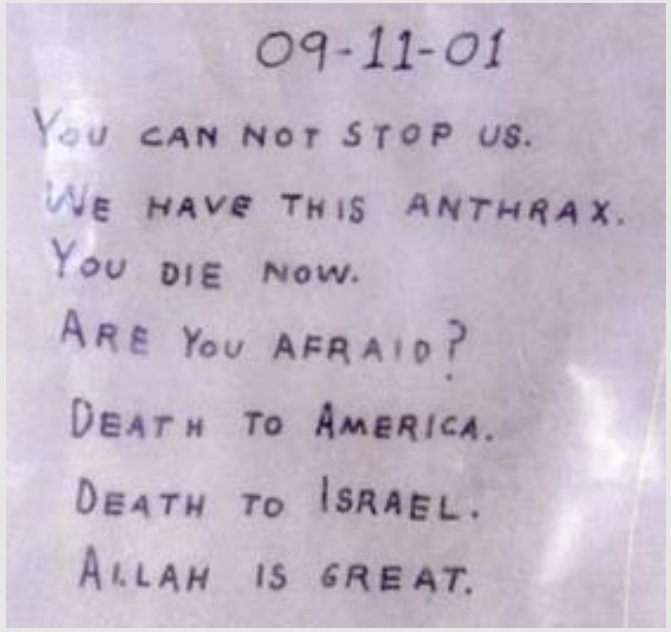


B. anthracis bacilli and spores

Spore wind distribution model

Meselson et al. The Sverdlovsk Anthrax Outbreak of 1979. Science. 1994

Amerithrax 2001



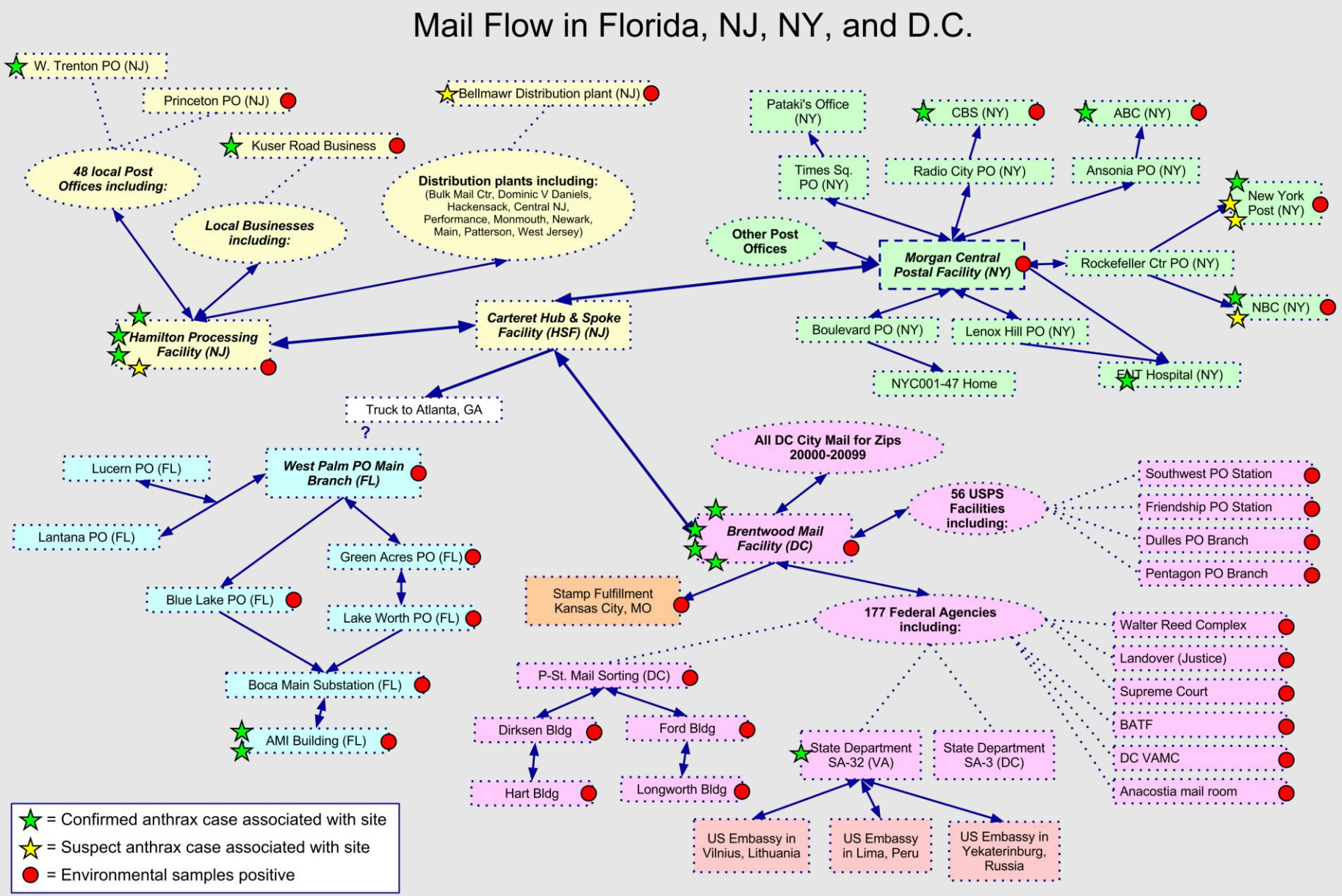
Beginning one week after the 9/11 terror attacks, letters containing anthrax spores were mailed to news media outlets and congressional offices in four states; Connecticut, Florida, New Jersey, and New York.

Resulted in **22 infections** including **5 deaths**

- Media Editor, postal workers, a hospital employee, and a resident

"Worst biological attack on US history"- FBI

Massive Investigation



The Worried Well

“worried well"—individuals seeking testing and preventive antibiotics despite having no known exposure

- The demand for healthcare and testing after a publicized bioterrorism event is often 20x greater than the need for actually impacted individuals.

- In Wisconsin alone, a state not involved in the attacks, we received thousands of “suspicious white powders” for anthrax testing. None were positive.

CDC USDA **FEDERAL SELECT AGENT PROGRAM**

Search

Overview | Select Agents & Toxins | Compliance | Regulations & Policies | Forms | Resources | eFSAP

Select Agents > Select Agents & Toxins

Select Agents and Toxins List

Print

The following biological agents and toxins have been determined to have the potential to pose a severe threat to both human and animal health, to plant health, or to animal and plant products. An attenuated strain of a select agent or an inactive form of a select toxin may be excluded from the requirements of the Select Agent Regulations. Here is a list of excluded agents and toxins.

Download PDF [PDF – 362 KB]

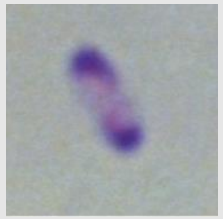
What makes something a Select Agent?

- High morbidity and/or mortality
- Little to no treatments/vaccines available
- Easily weaponized
  - Easily aerosolized
  - Easily spread in drinking water
  - Highly contagious
  - Persists in the environment

Select Agents

Bacterial

- Bacillus anthracis*
- Botulinum neurotoxin producing species of Clostridium*
- Bacillus cereus Biovar anthracis*
- Burkholderia mallei*
- Burkholderia pseudomallei*
- Coxiella burnetii
- Francisella tularensis*
- Rickettsia prowazekii
- Yersinia pestis*



Toxins

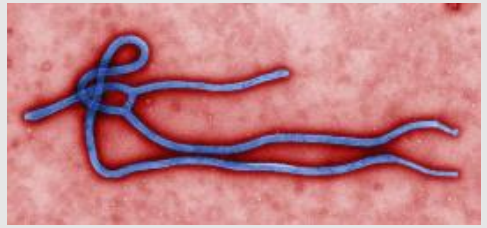
- Ricin
- Saxitoxin
- Staphylococcal enterotoxins A,B,C,D,E subtypes
- T-2 toxin
- Tetrodotoxin

https://www.selectagents.gov/SelectAgentsandToxinsList.html

* Tier 1 agent

Viral

- Hendra virus
- Nipah virus
- Rift Valley fever virus
- Venezuelan equine encephalitis virus
- Crimean-Congo haemorrhagic fever virus
- Eastern Equine Encephalitis virus
- Ebola virus*
- Lassa fever virus
- Lujo virus
- Marburg virus*
- Monkeypox virus (Clade I)
- 1918 Spanish flu
- SARS-associated coronavirus (SARS-CoV)
- South American Haemorrhagic Fever viruses:
  - Chapare virus
  - Guanarito virus
  - Junin virus
  - Machupo virus
  - Sabia virus
- Tick-borne encephalitis complex (flavi) viruses:
  - Far Eastern subtype
  - Siberian subtype
- Kyasanur Forest disease virus
- Omsk hemorrhagic fever virus
- Variola major virus (Smallpox virus)*
- Variola minor virus (Alastrim)*



Tier 1 Human Agents

Bacterial

- *Yersinia pestis*
- *Bacillus anthracis*
- *Bacillus cereus* Biovar *anthracis*
- *Burkholderia mallei*
- *Burkholderia pseudomallei*
- *Francisella tularensis*
- Botulinum neurotoxin-producing *Clostridium*

Toxins

- Botulinum neurotoxins

Viral

- Nipah virus
- Ebolavirus family
- Marburg virus family
- Variola major (Smallpox)
- Variola minor (Alastrim)

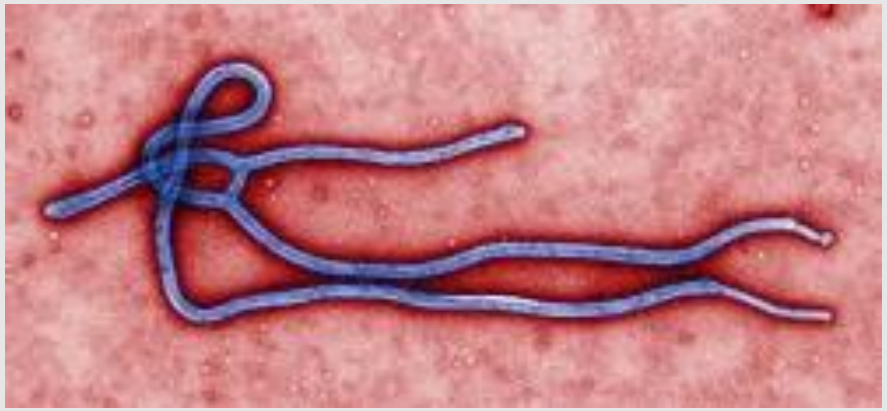
Hemorrhagic Fever Viruses

*Select Agent

Family	Genus	Species	Common Name	Human to human spread	Treatment	Vaccine	Mortality
Filovirus	Orthoebolavirus	*zairense*	Zaire ebolavirus	Yes	Yes	Yes	25-90%
		sudanense	Sudan ebolavirus	Yes	No	No	25-90%
		bundibugyoense	Bundibugyo ebolavirus	Yes	No	No	25-50%
		taïense "Côte d'Ivoire"	Taï forest ebolavirus	unknown	No	No	100% (1 case)
		restonense	Reston ebolavirus	No	No	No	no cases
		bombaliense	Bombali ebolavirus	unknown	No	No	no cases
	Orthomarburgvirus	*marburgense*	Marburg	Yes	No	No	20-90%
		marburgense	Ravn	Yes	No	No	50-60%
Arenavirus	Mammerenavirus	*Lassa mammarenavirus*	Lassa fever virus	Yes	Yes	No	1%, 95% miscarriage
		Lujo mammarenavirus	Lujo virus	Yes	No	No	80%
		Argentinian mammarenavirus	Junin virus	Yes	No	Yes	15-30%
		Mammarenavirus chapareense	Chapare virus	Yes	No	No	40-60%
		Mammarenavirus brazilense	Sabiá virus	presumed	No	No	10-50%
		Machupo mammarenavirus	Machupo virus	rare	No	No	20-35%
		Mammarenavirus guanaritoense	Guanarito virus	Presumed/rare	No	No	23-33%
Hantavirus	Orthohantaviruses	*Hantaviruses*	Hantaviruses	Andes strain	No	No	1-40%
Nairovirus	Orthonairovirus	*Orthonairovirus haemorrhagicae*	Crimean-Congo Hemorrhagic Fever virus	Yes	No	No	10-40%
Phenuvirus	Phlebovirus	*Phlebovirus riftense*	Rift Valley Fever virus	No	No	No	1-10%
Flaviviridae	Orthoflavivirus	*Orthoflavivirus kyasanurense*	Alkhurma hemorrhagic fever virus	No	No	No	1-25%
		Kyasanur Forest Disease virus	Kyasanur Forest Disease virus	No	No	Yes	2-10%
		Orthoflavivirus omskense	Omsk Hemorrhagic Fever virus	No	No	No	0.5-3%
		Orthoflavivirus denguei	Dengue virus	No	No	Yes	1-20%
		Orthoflavivirus flavi	Yellow Fever virus	No	No	Yes	3-7.5%
Paramyxoviruses	Henipavirus	*Henipavirus hendraense*	Hendra virus	No	No	Yes	57%
		Henipavirus nipahense	Nipah virus	Yes	No	No	40-75%

Ebola

- Two Treatments –Antibody based
  - October 2020 – Immazab
  - December 2020 – Ebanga
- Two Vaccines
  - December 2019 – Ervebo
  - July 2020 – Zabdeno / Mvabea



***Only approved for Zaire strain!**

Filoviruses

Family	Genus	Species	Common Name	Human to human spread	Incubation	Treatment	Vaccine	Mortality
Filovirus	Orthoebolavirus	*zairense*	Zaire	Yes	2-21 days	Yes	Yes	25-90%
		sudanense	Sudan	Yes	2-21 days	No	No	25-90%
		bundibugyoense	Bundibugyo	Yes	2-21 days	No	No	25-50%
		taïense "Côte d'Ivoire"	Taï forest	unknown	2-21 days	No	No	100% (1 case)
		restonense	Reston	No	NA	No	No	no cases
		bombaliense	Bombali	unknown	unknown	No	No	no cases
	Orthomarburgvirus	*marburgense*	Marburg	Yes	2-21 days	No	No	20-90%
		marburgense	Ravn	Yes	2-21 days	No	No	50-60%

Response

Laboratory Response Network

Created by the CDC to respond to Select agents, biological warfare, and emerging threats.

- Producing data for smart public health decisions
- Maintaining and improving national laboratory capacity
- Strengthening national security
- Testing for old and new diseases
- Ensuring high standards and enabling high confidence in results

LRN-B Structure

The LRN-B was founded in 1999 by CDC, FBI and APHL to coordinate laboratory response to biological, chemical, radiological threats and other high priority public health emergencies, including emerging infectious diseases.

National Laboratories

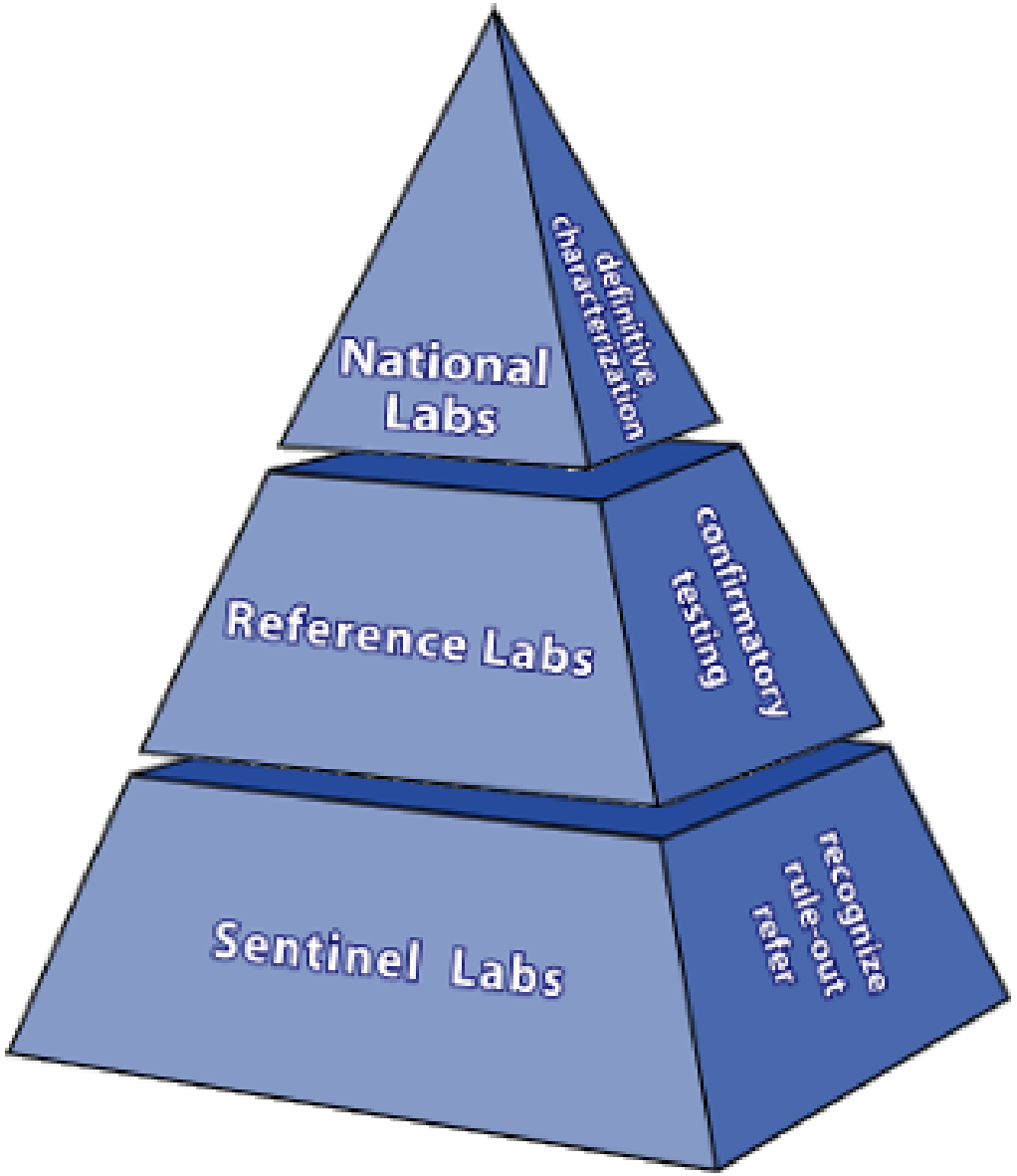
National labs, including the CDC, US Army Medical Research Institute of Infectious Diseases (USAMRIID), and the Naval Medical Research Center (NMRC), are responsible for specialized strain characterization, bioforensics, biothreat agent activity and handling of highly infectious biological agents.

Reference Laboratories

Reference labs, including state and local public health, military, veterinary, agriculture, food and water testing laboratories, are responsible for investigation and confirmatory testing. Facilities located in Australia, Canada, the United Kingdom, Mexico and South Korea serve as international reference laboratories.

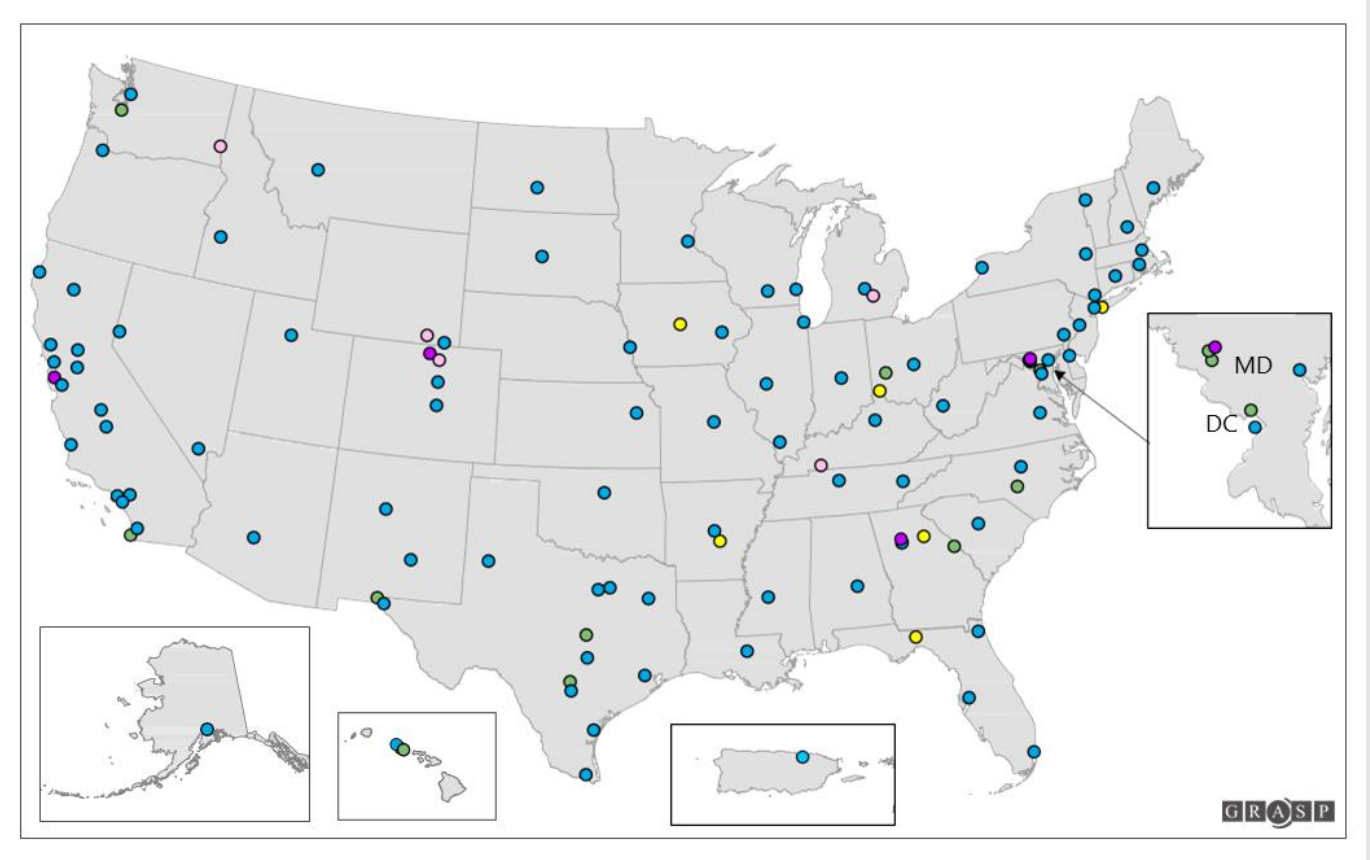
Sentinel Laboratories

Sentinel labs, comprised of hospital-based and commercial laboratories, are responsible for the early detection and the rule-out or referral of potential biothreat agents.



LRN-B Labs Across the US

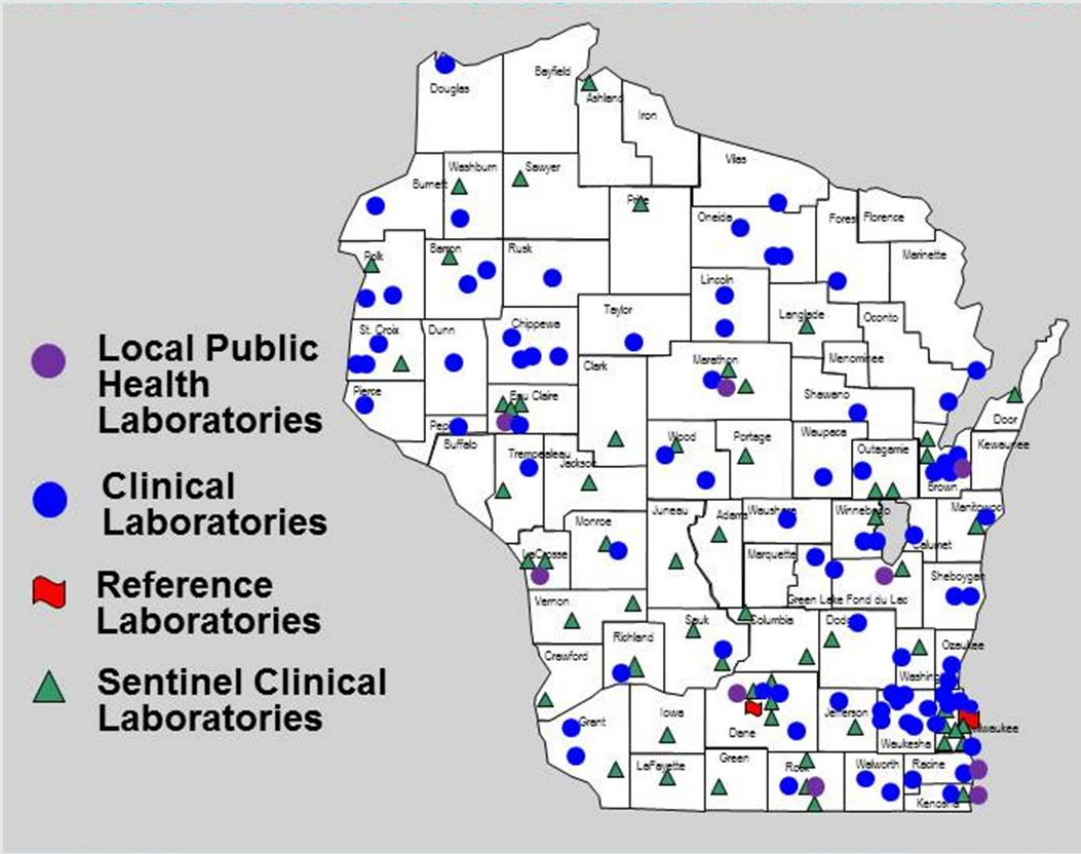
- 120+ Member Labs
- 84% of Americans live within 100 miles of a lab
- 45 distinct tests for biological threats
- 5,500 specimens processed in 2023



*At least one in every state, 120+ total labs

Wisconsin Clinical Laboratory Network (WCLN)

- Comprised of 152+ laboratories
- Facilitated by the Wisconsin State Laboratory of Hygiene
- Coordinator: Nick Zumwalde, PhD



We Test Suspect Select Agents

Environmental Samples	Patient Specimens	Clinical Isolates
White powders	Tissue, swabs, fluids	Pure cultures
		
HAZMAT Teams in the Field	Medical teams in a Hospital	Laboratorians
		

Test Methods

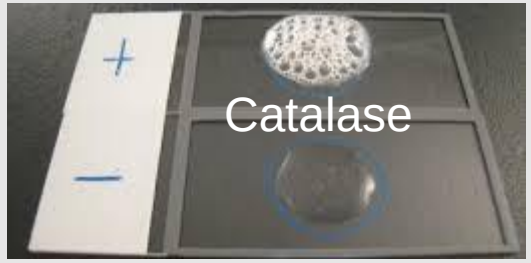
Biosafety level 3

Biosafety level 4

Microscopy

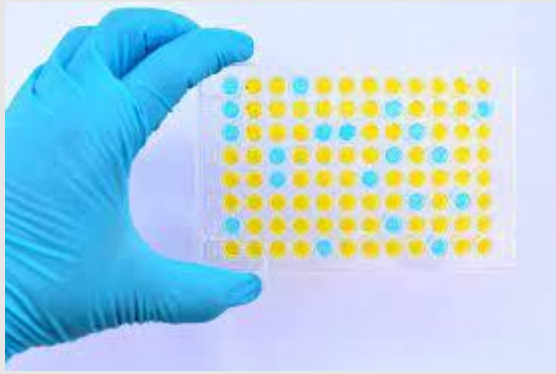
Culture

Biochemicals



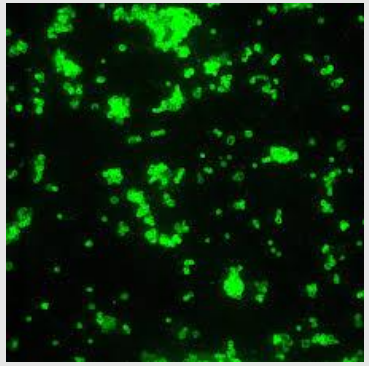
Results in 4 hours to 5 days

ELISA



PCR

DFA



Current Events

W.H.O. Declares Ebola Outbreak a Global Health Emergency

Case

- It’s Friday at 4pm and a call comes in to my desk:

  “We have a suspect Ebola patient, what should we do?”

- First let’s gather some information:
  - 8 year old male
  - Recent travel to the Africa
  - Presented to the ER with fever
  - Recent history of a bloody nose

Case continued

Response Activated

- I call key contacts at the state Department of Health (DHS)
- DHS calls the CDC special pathogens emergency line
- We all get on a zoom call with the members from the hospital

Information Collected- Had traveled in a city with an active outbreak

- Risk factors, exposure history, clinical findings, timeline, close contacts, patient isolation, test results

Case Determination – CDC decides if this is a true suspect case

Consultation

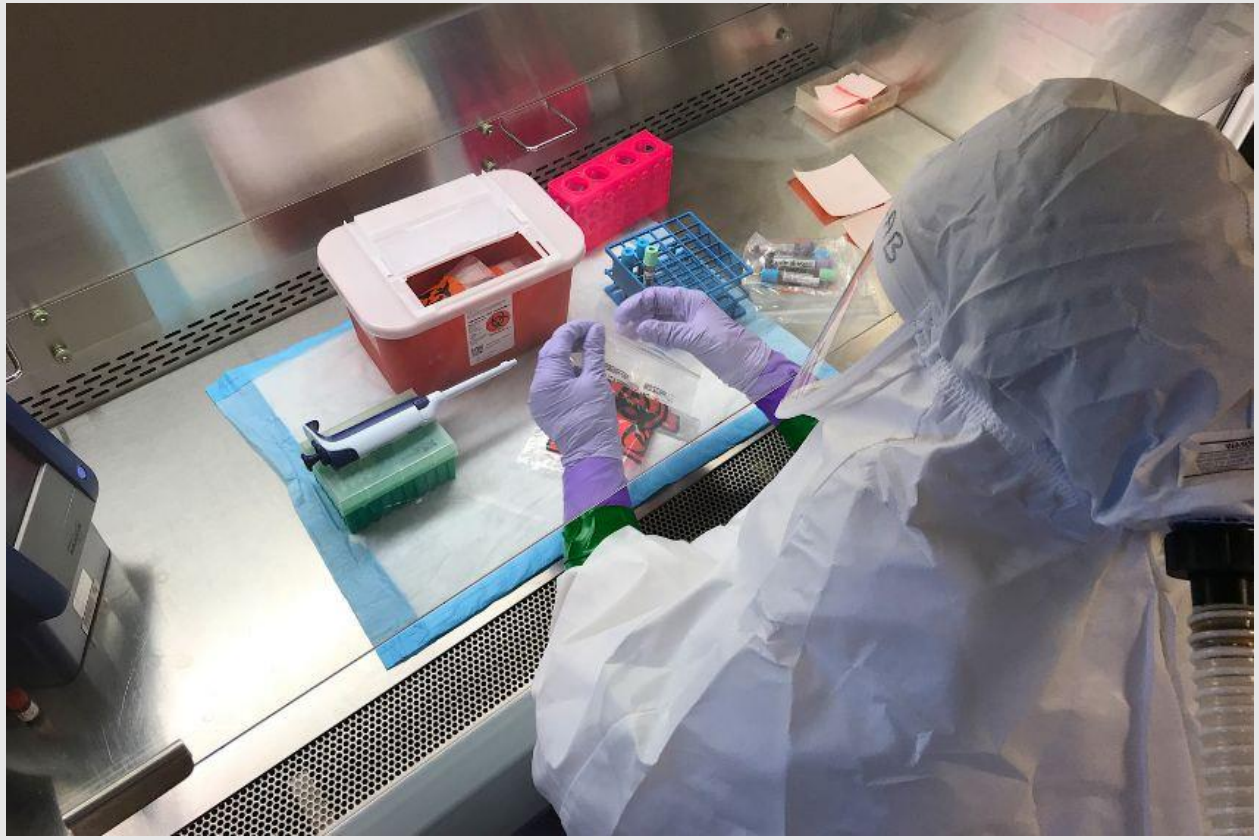
- CDC physicians consult about treatment, isolation, PPE, and specimen collection
- WSLH LRN-B consults on available testing and specimen logistics
- We develop a plan and execute

Case continued

- The patient is placed in the highest containment room available
- Nurses wearing full PPE carefully collect blood
- The blood is contained, surface decontaminated, Category A packaged, and transported to the WSLH.

Case continued

- The package is opened in the BSL3 under full containment procedures.
- LRN-B PCR protocols are used to test for Ebolavirus
- Results come back negative!



Final diagnosis: Malaria!

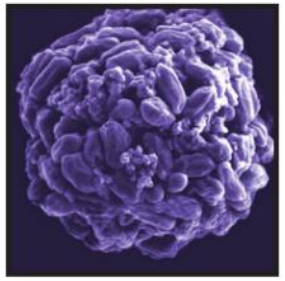
New Method

BioFire Torch

FilmArray-
Microfluidic, array based, multiplexed PCR

Global Fever Special Pathogen Panel

1 Test. 16 Targets. In 50 Minutes.

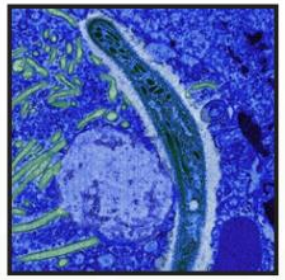


Bacteria

Bacillus anthracis
Francisella tularensis
Leptospira spp.
Yersinia pestis

Viruses

Chikungunya virus
Crimean-Congo hemorrhagic fever virus
Dengue virus (serotypes 1, 2, 3 and 4)
Ebolavirus spp. (Bundibugyo, Reston, Sudan, Taï Forest, Zaire)
Lassa virus
Marburgvirus
West Nile virus
Yellow fever virus



Protozoa

Leishmania spp.
Plasmodium spp.
Plasmodium falciparum
Plasmodium vivax/ovale

Fast. Easy. Comprehensive Testing.

Syndromic testing provides a streamlined workflow with fast, comprehensive results.

0.2 mL (200 µL)
of whole blood

2 minutes
hands-on time

Results in
50 minutes

Comprehensive
results in a single report

Clinical Performance Summary

Analyte	PPA (Sensitivity)	NPA (Specificity)
Bacillus anthracis	100%*	100%
Francisella tularensis	100%*	100%
Leptospira spp.	93.8%	99.8%
Yersinia pestis	100%*	100%
Chikungunya virus	100%	99.9%
Crimean-Congo hemorrhagic fever virus	98%	100%
Dengue virus (serotypes 1, 2, 3, and 4)	94%	100%
Ebolavirus spp.	100%*	100%

Analyte	PPA (Sensitivity)	NPA (Specificity)
Lassa virus	100%*	100%
Marburgvirus	99%*	100%
West Nile virus	100%*	99.7%
Yellow fever virus	98%*	100%
Leishmania spp.	100%	100%
Plasmodium spp.	98.5%	99.2%
Plasmodium falciparum	92.7%	99.8%
Plasmodium vivax/ovale	92.7%	100%

Data established during a prospective clinical study, except where indicated.
*Performance was established using contrived specimens. See panel specific IFU for details.

All Select Agents detected will get confirmation testing

What This Means

- Results for high consequence pathogens will be available faster than ever before.
- Reduced hands–on time is easier and safer for lab staff, reducing risks when testing at 2am.
- The panel expands our test menu to include more hemorrhagic fever viruses.
- Faster results translates to patients getting appropriate treatment faster, reduced risk of transmission, and faster public health response to contain the spread.

Summary

- **Bioterrorism is an enduring threat** that continues to evolve, with Select Agents representing the organisms and toxins of greatest concern despite international efforts to limit their use.
- **Select Agent Programs and the LRN-B provide critical public health infrastructure**, enabling rapid, local, and comprehensive testing to support both response and reassurance during suspected events.
- **Advancing diagnostic methods** are strengthening preparedness, expanding testing capacity and reducing time to results to improve patient outcomes and public health response.