

# Coincidence or Cluster:

## Collaboration Between Clinical Microbiology and Public Health Laboratories Impacting Population Health

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# Disclosures

- No relevant disclosures for this presentation



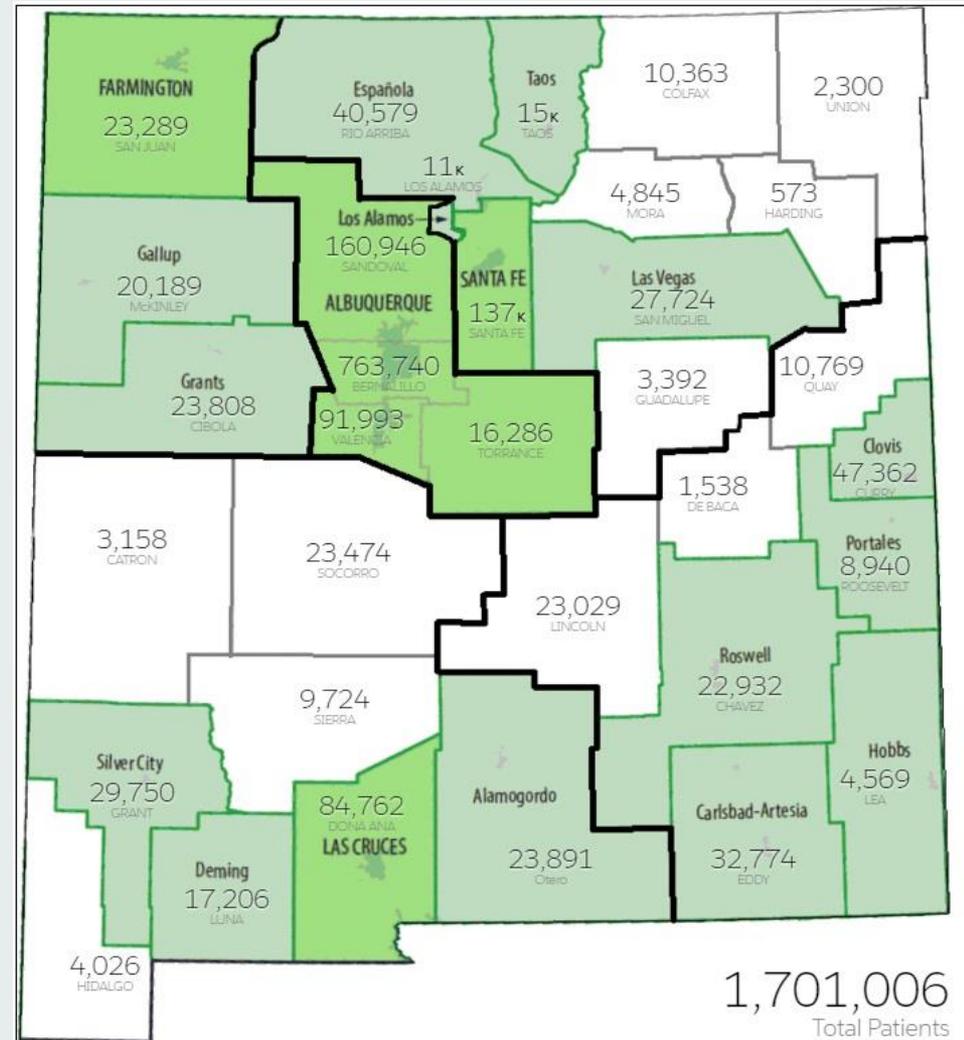
# Objectives

- Attendees of this symposia will be able to:
  - Define the role of the clinical laboratory in the public health setting
  - Describe the unique role of the clinical laboratory in detecting unusual patterns of infections
  - Understand how results from the clinical laboratory can be used to impact population health



# The Challenge of Laboratory Services in New Mexico

- Large sparsely populated geographical areas
- Remote locations
- Socioeconomic conditions
- Specimen collection and quality control



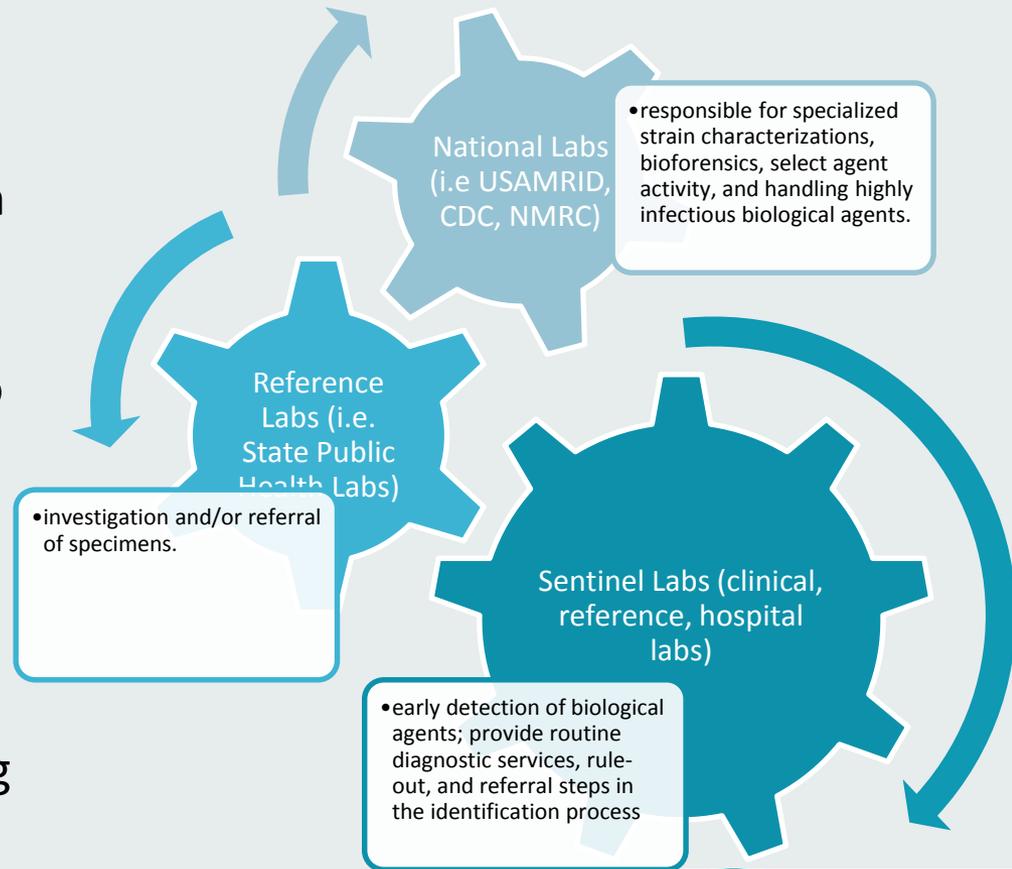
# TriCore Reference Laboratories

- 7.8 million tests per year
- 11 hospital-based rapid response laboratories
- Hospital Lab for University of New Mexico Hospital and Presbyterian Hospital Systems
- >25 patient care centers
- Employs ~1,100 individuals



# Laboratory Response Network

- LRN is a national security asset that, with its partners, will develop, maintain and strengthen an integrated domestic and international network of laboratories to respond quickly to biological, chemical, and radiological threats and other high priority public health emergencies needs through training, rapid testing, timely notification and secure messaging of laboratory results.

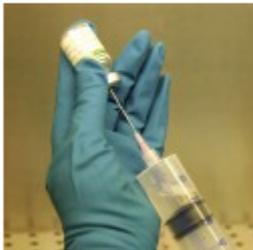


# Identifying Biological Threats

## ABC News: Fungal Meningitis Injections. Several Deaths

by [ANewDayANewMe](#)

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has been traced back to a *Center*, which has since closed. The outbreak may spread because of clinics in 23 different states.



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By Faith  
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## Two More Hospitals Report 'Superbugs' on Endoscopes

by MAGGIE FOX

HEALTH  
MAR 5 2015, 12:27 AM ET

Carbapenem-resistant Enterobacteriaceae (CRE) bacteria.  Handout / Getty Images



Brandi Chastain  
brain

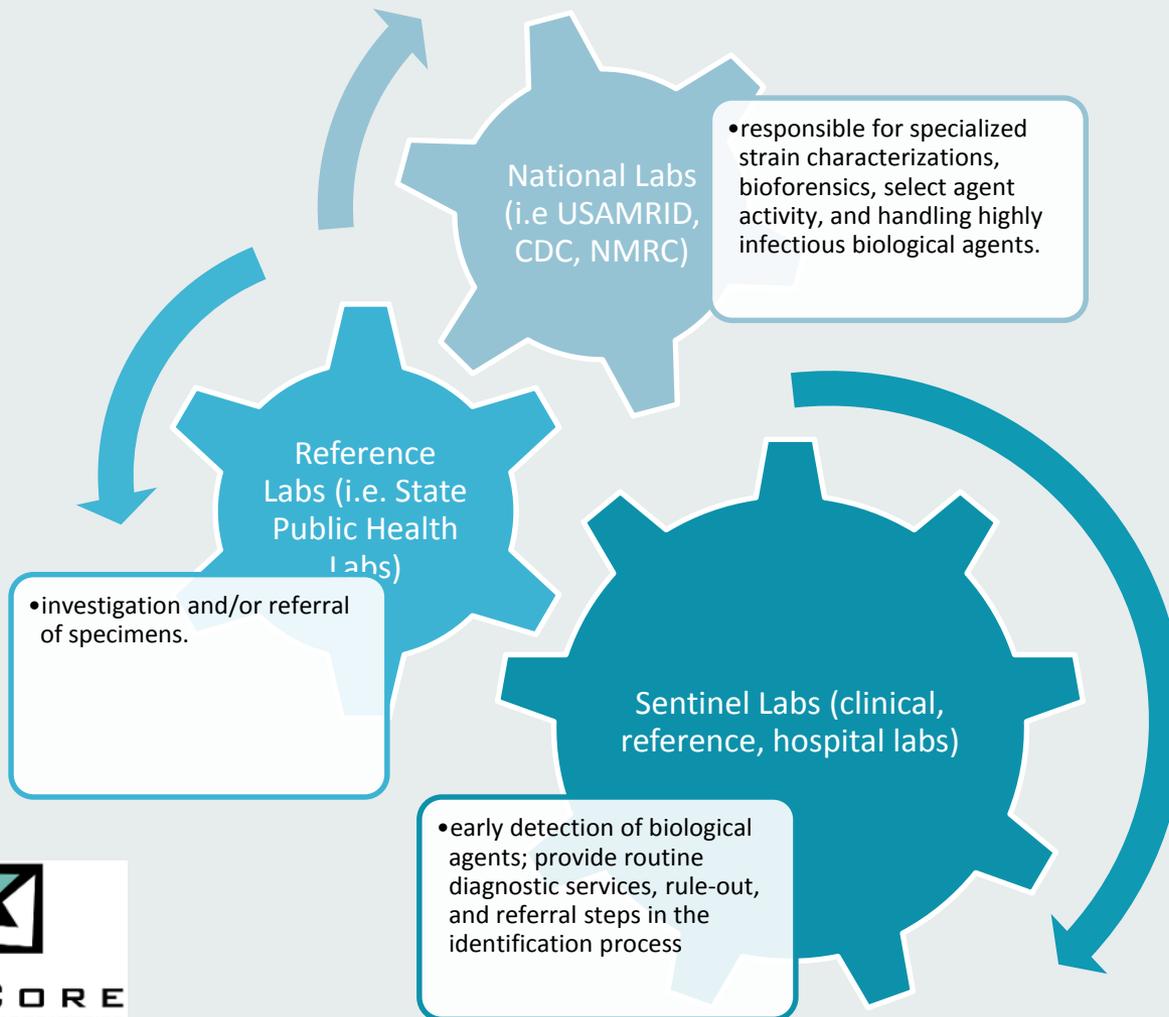
Today's Mortgage

3.01% UNM

APR SCIENCES

Calculate New Pay CENTER

# How to start the gears turning?



Select Agent: n=1

State Reportable List:  
n= 1 – a few

Lab notices something weird  
n= ?

# Cluster or Coincidence

- Cluster: unusual aggregation, real or perceived, of health events that are grouped together in time and space and that are reported to a health agency
- Coincidence: the occurrence of events that happen at the same time by accident but seem to have some connection (Merriam-Webster Definition)



# Investigation of a Cluster

- Stage 1: Initial Contact and Response
- Stage 2: Assessment
- Stage 3: Major Feasibility Study
- Stage 4: Statistical and Epidemiologic Techniques



# CASE 1



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# One day on rounds...

- December 2013

Technologist: “Dr. Culbreath, I have an *Elizabethkingia meningoseptica* from a sinus culture, isn’t that interesting?”

Dr. Culbreath: “We also had a positive sinus culture for *E. meningoseptica* last week!”



# *E. meningospetica*

- Formerly known as *Chryseobacterium meningosepticum*
- Gram-negative, non-fermenting oblicage aerobe
- Widely distributed in the environment
- Most commonly, infections associated with neonatal meningitis



# *E. Meningospetica* in Adult Outbreaks

- Associated with respiratory infections including ventilator-associated infections
  - Tap water and environmental sources
    - Misuse of tap water in patient care
  - Equipment
    - Mechanical ventilation, catheters
  - Solutions
    - saline, antiseptic solutions
  - Often multiple *E. meningoseptica* strains isolated from environment, not always associated with the outbreak



# Laboratory Investigation

- Culture 1: 11/6/2013 osteomeatal unit
- Culture 2: 11/20/2013 ethmoid sinus
- Different facilities in Albuquerque, NM
- Since 2010, 1 previous positive for this organism from a chest wound



# Coincidence or Cluster?

- **Coincidence** – two isolates don't (necessarily) make a cluster
- **Cluster** – it's small, but is it the beginning of a cluster/outbreak?



# Public Health Investigation

- Both patients were using nasal irrigation products including tobramycin, budesonide, and a saline solution (isotonic powder mixed with water).
- Both patients had history of chronic sinus problems with associated symptoms of congestion and sinus pain/pressure.
- Neither patient was severely ill or required hospitalization (i.e., no bacteremia, no meningitis).
- The tobramycin used by both patients came from the same compounding pharmacy.

*Coincidence or Cluster?*



# Investigation of Compounding Pharmacy

- Local Board of Pharmacy conducted an onsite visit
- The products used by the patients had different lot numbers
- No violations or other cause for concern raised by the onsite visit

*Coincidence or Cluster?*

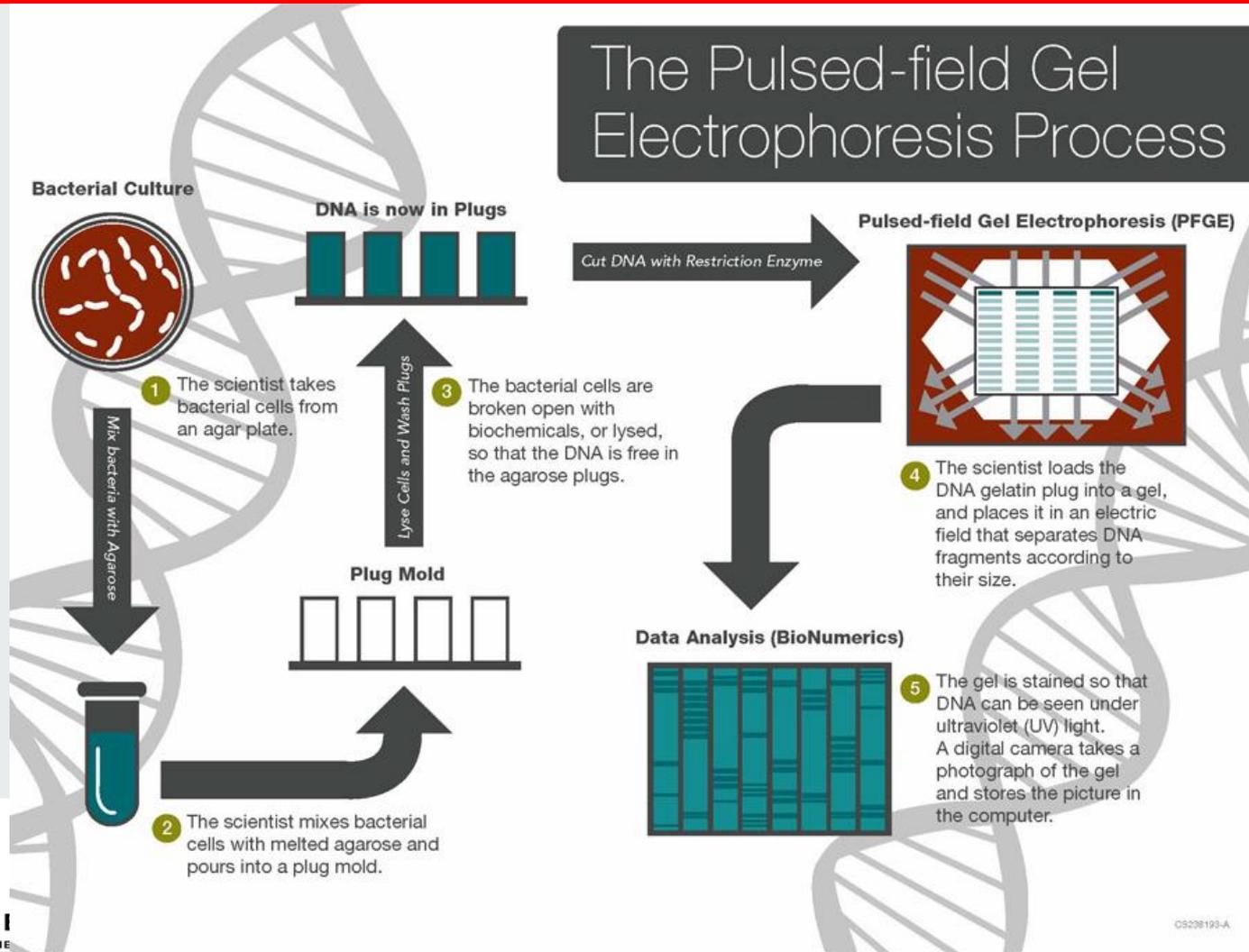


# How do we determine if isolates are the same?

- Antibiogram typing – most valuable first-line method
  - Low sensitivity
- PFGE – Pulse field gel electrophoresis
  - Good sensitivity to related organisms
  - Labor intensive, specialized instruments and technologist, long turn-around-time



# Bacterial Strain Typing: PFGE



# Interpretation of PFGE Banding Patterns

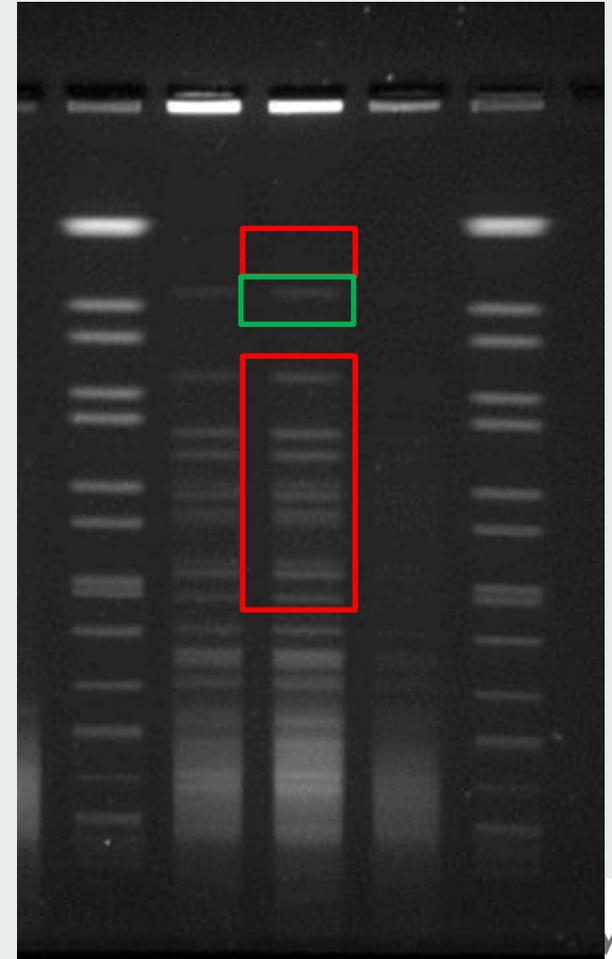
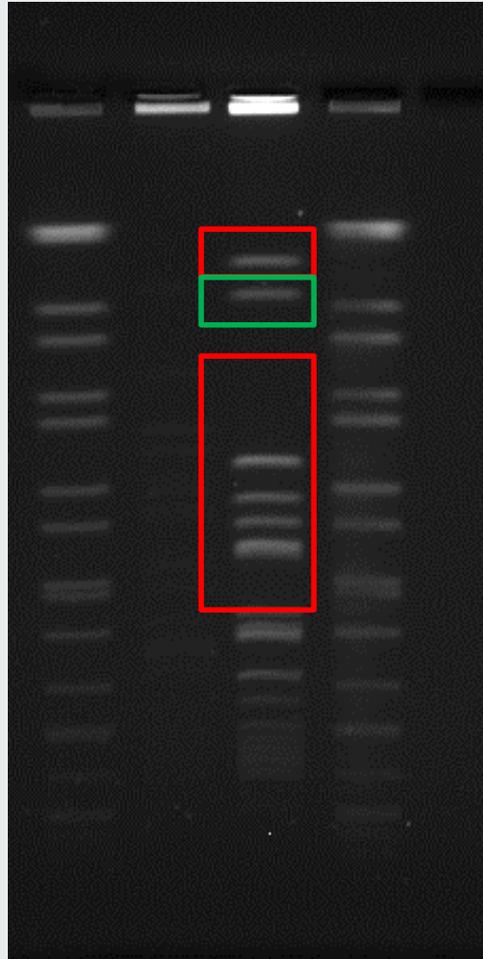
TABLE 2. Criteria for interpreting PFGE patterns

Category	No. of genetic differences compared with outbreak strain	Typical no. of fragment differences compared with outbreak pattern	Epidemiologic interpretation
Indistinguishable	0	0	Isolate is part of the outbreak
Closely related	1	2–3	Isolate is probably part of the outbreak
Possibly related	2	4–6	Isolate is possibly part of the outbreak
Different	$\geq 3$	$\geq 7$	Isolate is not part of the outbreak



# Both Isolates Had PFGE Typing

- Isolates were different and **not** considered to be epidemiologically related
- Upon interviews of the two patients, both used unboiled/unfiltered tap water in preparing the nasal irrigation solution



# Recommendations

- Healthcare providers and patients were contacted to educate them not to use tap water for nasal irrigation unless it has been boiled or filtered



# CASE 2



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# One day on rounds...

- April 2013
- “Dr. Culbreath, we have aerobic blood culture bottles from *two different patients* collected at the *same facility* on the *same day* that are both positive for *B. cepacia*.”



# Coincidence or Cluster?

- **One is a false positive:** One patient has *B. cepacia* one doesn't, one set was mislabeled,
- **Both True Positives:** both patients have *B. cepacia*
- **Both false positives:** neither has *B. cepacia*, blood culture bottles are contaminated



# *Burkholderia cepacia*

- Glucose non-fermenting Gram-negative rod
- Occasional opportunistic pathogen
  - Chronic granulomatous disease (CGD) and cystic fibrosis (CF)
- Nosocomial outbreaks
- Pseudo-outbreaks: Contamination of blood culture systems or disinfectants



# Outbreaks with *B. cepacia*

- Non-Cystic Fibrosis Adults
  - Bacteremia due to contaminated compounded solutions
  - Respiratory infection due to contaminated inhaled nebulized medications
  - Outbreaks in immunocompromised patients are common and can have increased mortality
  - May be polyclonal and source difficult to isolate



# Laboratory investigation

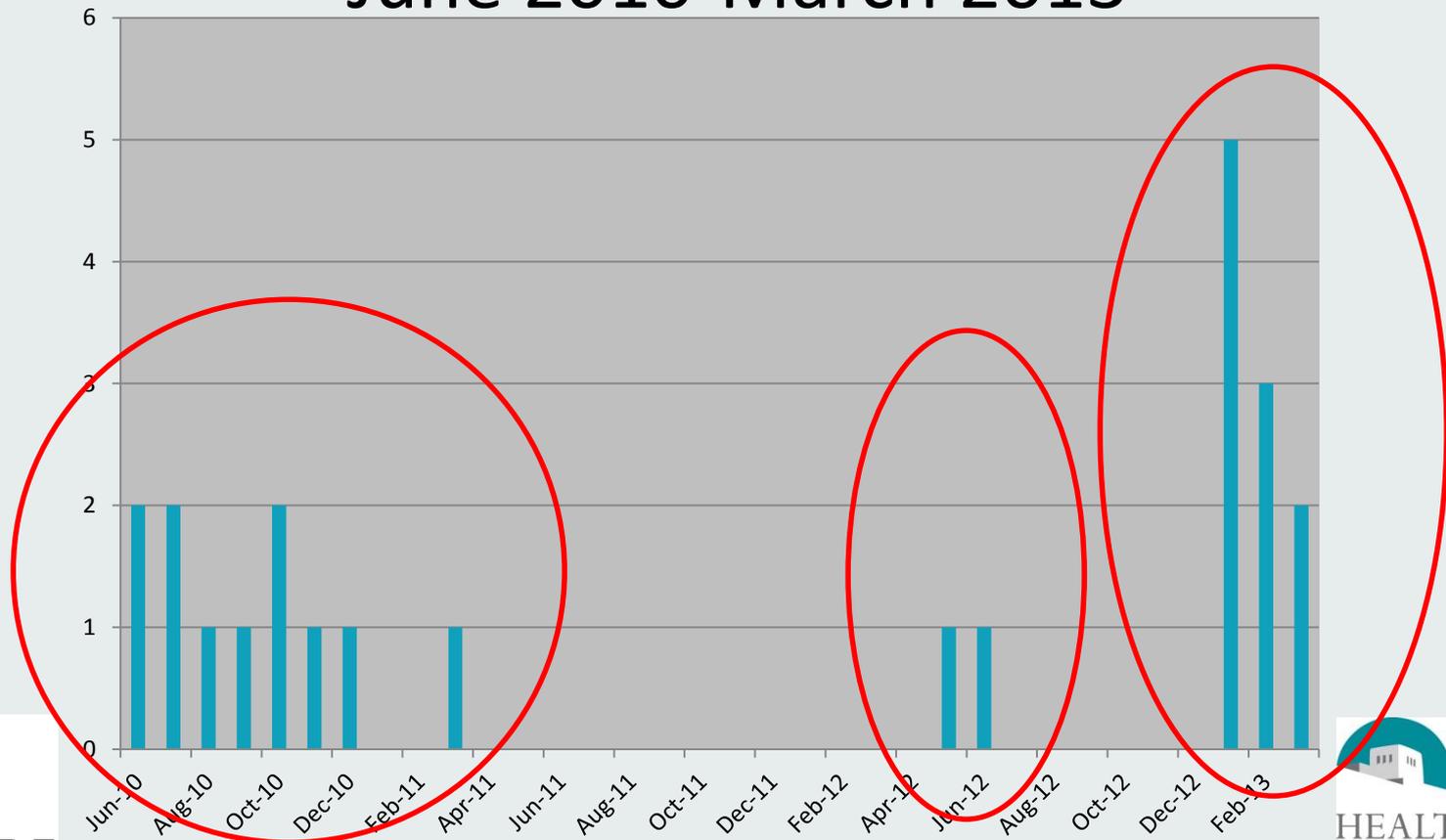
- Labels from the laboratory match
- Provider assures the labels were correct at their facility
  - Provider states the patients seen are all late-stage cancer patients and highly immunocompromised
  - Provider uses provider-mixed infusions to support end of life care

*Coincidence or Cluster?*

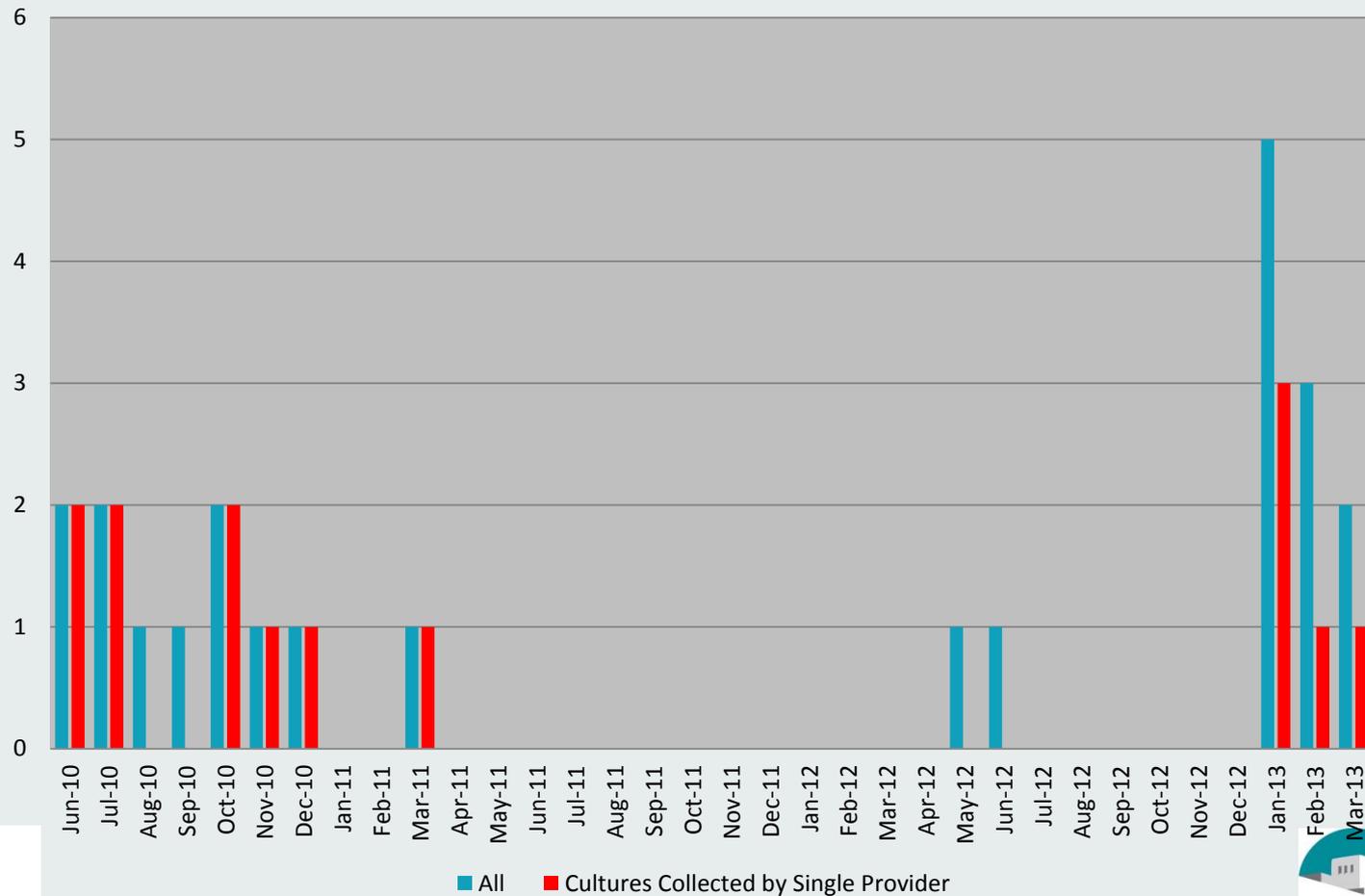


# Data from BD EpiCenter

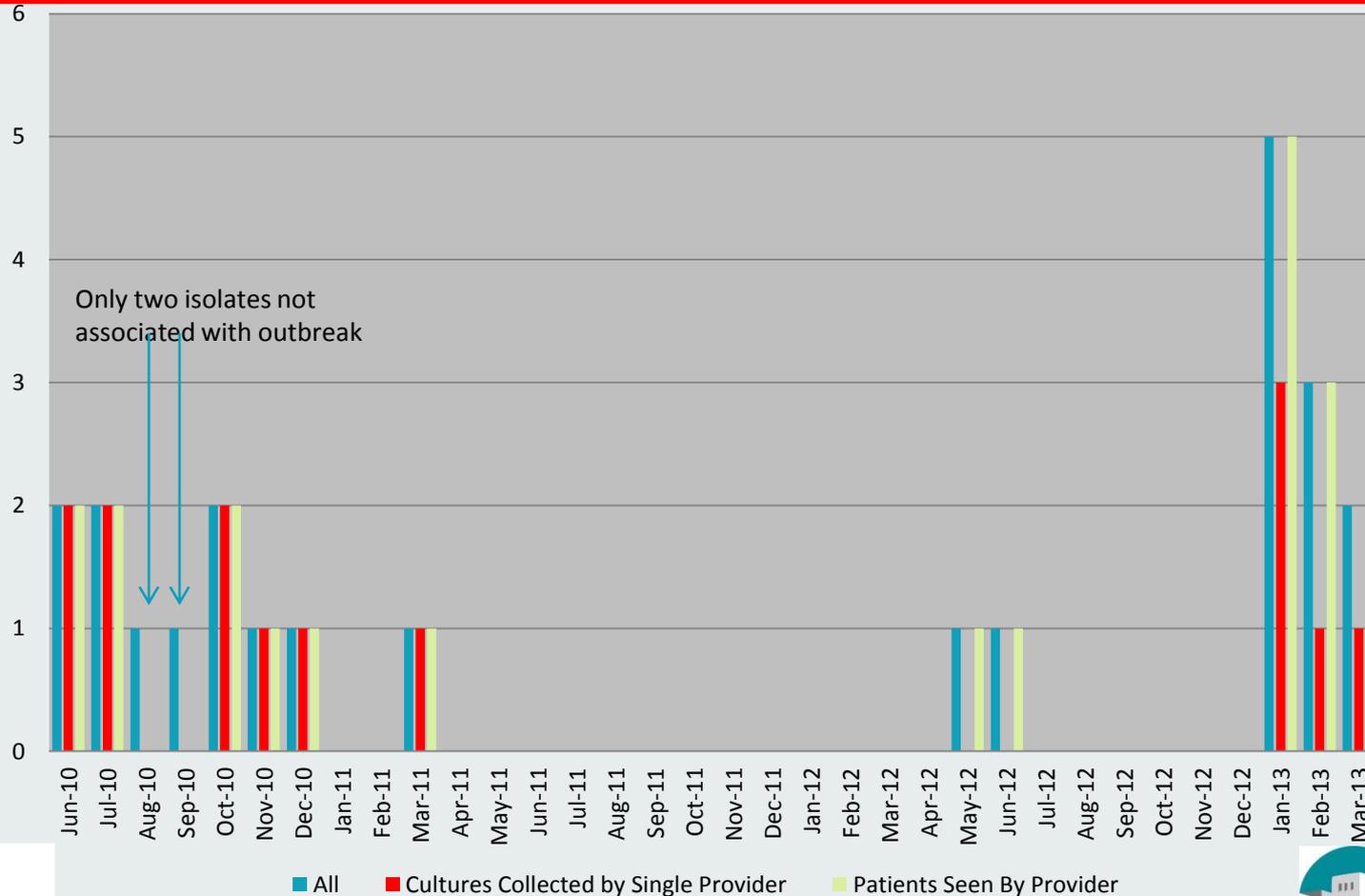
All positive blood cultures for *B. cepacia*  
June 2010-March 2013



# B. cepacia isolates from the blood collected at facility in question



# B. cepacia positive from blood collected at all other facilities



# What's next?

- Call the provider to prompt a change to practice
- Call Department of Health to initiate an investigation
- Call the local news station investigative reporter



# Department of Health Investigation Results

- 8 Patients
  - All female
  - Median age 50.8 years (26-62 years)
  - 7 patients noted to have carcinoma
    - Stage 4 renal cancer, stage 4 non-small cell lung cancer, stage 4 colon cancer, recurrent breast cancer, stage 4 breast cancer, ovarian cancer, adrenal leiomyosarcoma
  - 1 patient with chronic myalgias, fatigue, joint pain



# Medications Received

- 6 patients noted to have received IV “insulin potentiated therapy (IPT)”
  - Acyclovir, difulcan, glutathione, metronidazole, toradol, zantac, zofran, taxol, EDTA, vitamic C, fluorouracil, antiangiogenesis, oxaliplatin, erbitux, dextrose, dexamthasone, insulin, vinoreleben, and amino acids
- Other products administered via IV: paracelsus, indiba, MRS, “nutrition bag”, iron sulfated, bactrim, unasyn, benadryl



# Office Visits to Provider: **Red Flags**

- Medication storage refrigerator with a few personal food items, probiotics and vial of DMSA with patient name.
- None of the opened medication vials were marked with dates of opening
- Numerous medication vials had expiration dates that had passed (3 passed by 2-3 years)
- Vials that appeared to be single dose vials had been opened and contained remaining products

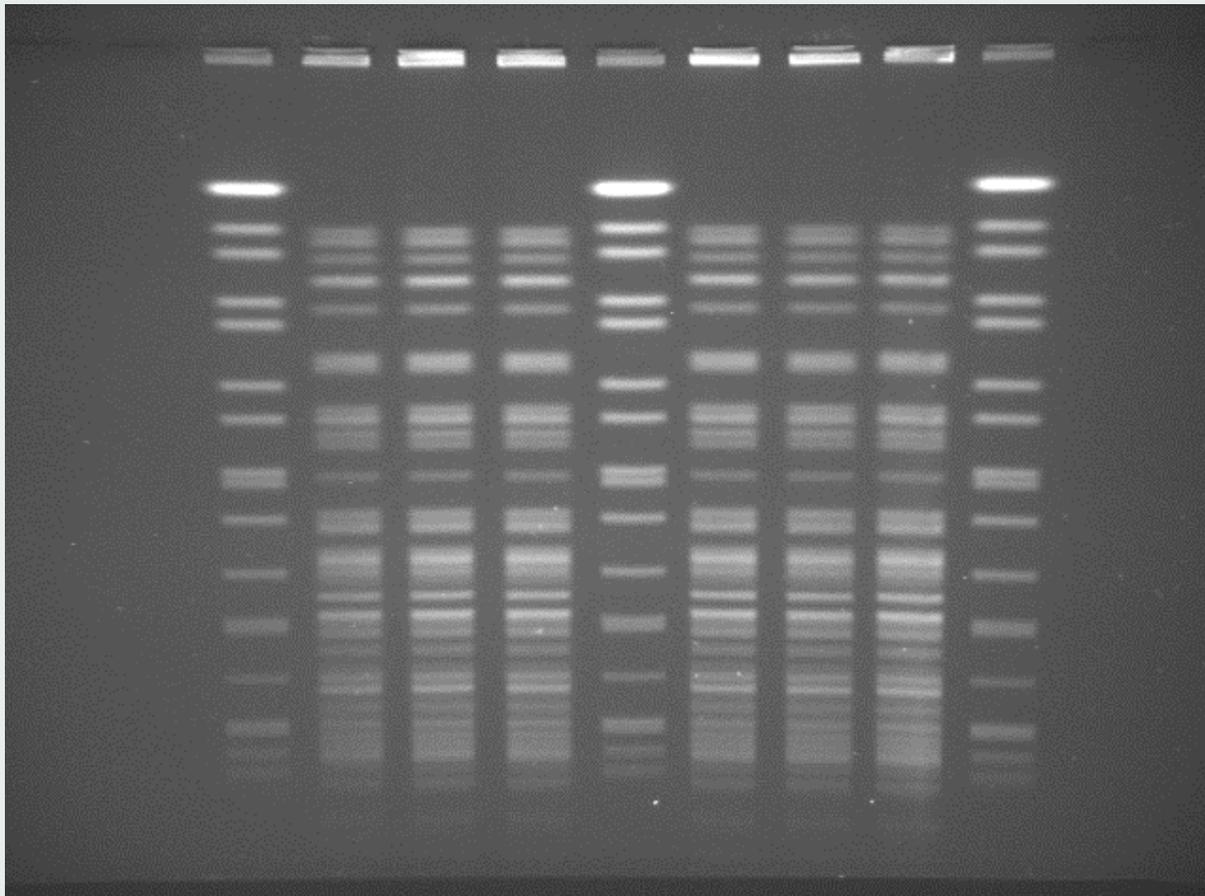


# Coincidence or Cluster: Analysis of Isolates

- Pulsed-Field Gel Electrophoresis (PFGE; XbaI)
  - Isolates from 2013 cluster were analyzed
  - 2 clinical isolates from CF patients not associated with the cluster
  - 1 isolate from throat swab from a cluster patient



# PFGE – Clinical Patient Isolates from 2013 Cluster



# PFGE Results

- All clinical isolates for 2013 cluster were identical among the patients tested
- The *B. cepacia* isolates from CF patients did not match the cluster isolates
- The *B. cepacia* isolated from the throat of one of the cluster patients did not match the cluster isolates



# The Smoking Gun

- *B. cepacia* was grown from an opened 30-mL vial of preservative free L-methionine stored in the refrigerator
- Banding pattern matched the clinical cluster isolates



# Infection Control Recommendations

- Follow storage, usage (single use vs. multi-use) and expiration date requirements for all medications
- Proper use of biohazard containers for discarding of medical equipment
- Suspend intravenous infusions until the assessment was completed.



# Patient Recommendations and Follow -Up

- Ongoing surveillance on all individuals receiving intravenous therapy for a minimum of 6 months
  - No additional *B. cepacia* were identified
- One patient death was noted approximately 5 months after the positive blood culture
- One patient referred to hospice care 1 month after positive blood culture
  - Patients had significant co-morbidities and these impacts could not be directly attributable to the *B. cepacia* infection.



# Laboratory's Role in Detecting Outbreaks

- Knowledge of LRN requirements for the clinical laboratory in rule-out of select agents
- Use of laboratory analytics to retrospectively analyze data for outbreak investigation
- Maintain repository of clinical isolates in the laboratory for retrospective analysis
- Keep your eyes open and your brain on!

