Multistate Outbreaks of *Burkholderia Cepacia* Complex Infections Due to Contaminated Medical Products

Matthew B Crist, MD, MPH
Medical Officer, Response Team
Division of Health Care Quality Promotion
Centers for Disease Control and Prevention

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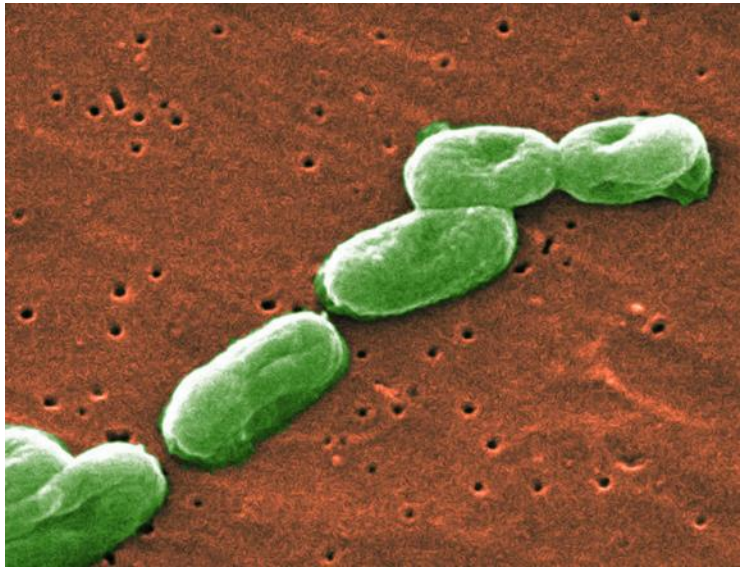
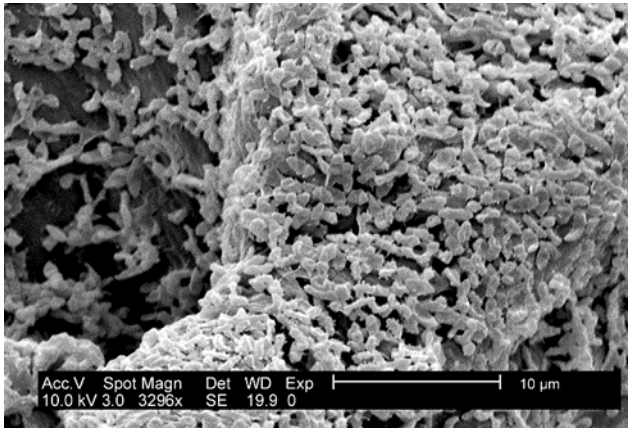
Burkholderia cepacia complex

- Group of gram negative rod bacteria
- Complex contains many species
- Ubiquitous in soil and water
- Colonize and cause pulmonary infections in cystic fibrosis patients
- Can cause healthcare-associated infections



Characteristics of *Burkholderia cepacia* complex

- Transmissible person to person or from environmental source
- Biofilm formation in water systems
- Intrinsic antimicrobial and preservative resistance
- Outbreaks associated with aqueous products



Initial Notifications

- CDC notified by TX Department of State Health Services afternoon of 5/3/2016
  - 15 cases of *Burholderia cepacia* complex (Bcc) in ICU patients at a pediatric hospital over 2 month period
  - Did not have cystic fibrosis
  - Various sites of infection: respiratory (majority), blood, urine
- Followed by notification from IL Department of Public Health on the morning of 5/4/2016
  - 4 cases of Bcc in ICU patients at a pediatric hospital over 1 month period
  - Did not have cystic fibrosis
  - Various sites of infection: respiratory (majority), blood, wound

Molecular Comparison

- Both hospitals had submitted isolates to Burkholderia Research Laboratory at the University of Michigan

- Isolates found to be indistinguishable by box PCR
  - Within each facility
  - Across the two facilities in different regions of the country

- Previously undescribed species within the Bcc

Initial Actions

- Notified FDA
- Began looking for common exposures across facilities
- Additional case/cluster finding
  - Became aware of a 3rd facility in CA that was also having a cluster of Bcc in pediatric critically ill patients
- Obtained isolates from the 3 facilities
  - Isolates across facilities found to be indistinguishable by pulsed field gel electrophoresis (PFGE)
- CDC issued a national call for clusters initially focusing on clusters of Bcc in non-cystic fibrosis pediatric ICU patients

Developments

- Notified of a cluster in an adult ICU
  - PFGE also showed the Bcc outbreak strain
- Second PFGE pattern emerged
  - Different from the primary pattern but was seen in multiple states
  - Patterns were labeled Pattern A and Pattern B
- Continued to be notified of additional clusters
- Coordinated with state and local health departments
  - Obtained exposure information
  - Facilitated isolate submission to the CDC Clinical and Environmental Microbiology Laboratory

Investigating Exposures

- Patient care products
  - Oral care
  - Skin care
- Ventilator Products
  - Circuits
  - Sterile water for inhalation
  - Humidifiers
- Common procedures
- Medications
  - Inhaled medications
  - Intranasal
  - Oral medications

Liquid Docusate

- TX facility sent products and medications to reference laboratory for culture
- On 6/24/16 liquid docusate produced by PharmaTech and distributed by Rugby tested positive for Bcc
- CDC confirmed culture findings
- Isolate indistinguishable from outbreak strain by PFGE
- CDC issued a nationwide health alert recommending facilities immediately suspend use of all oral liquid docusate

Case Definition

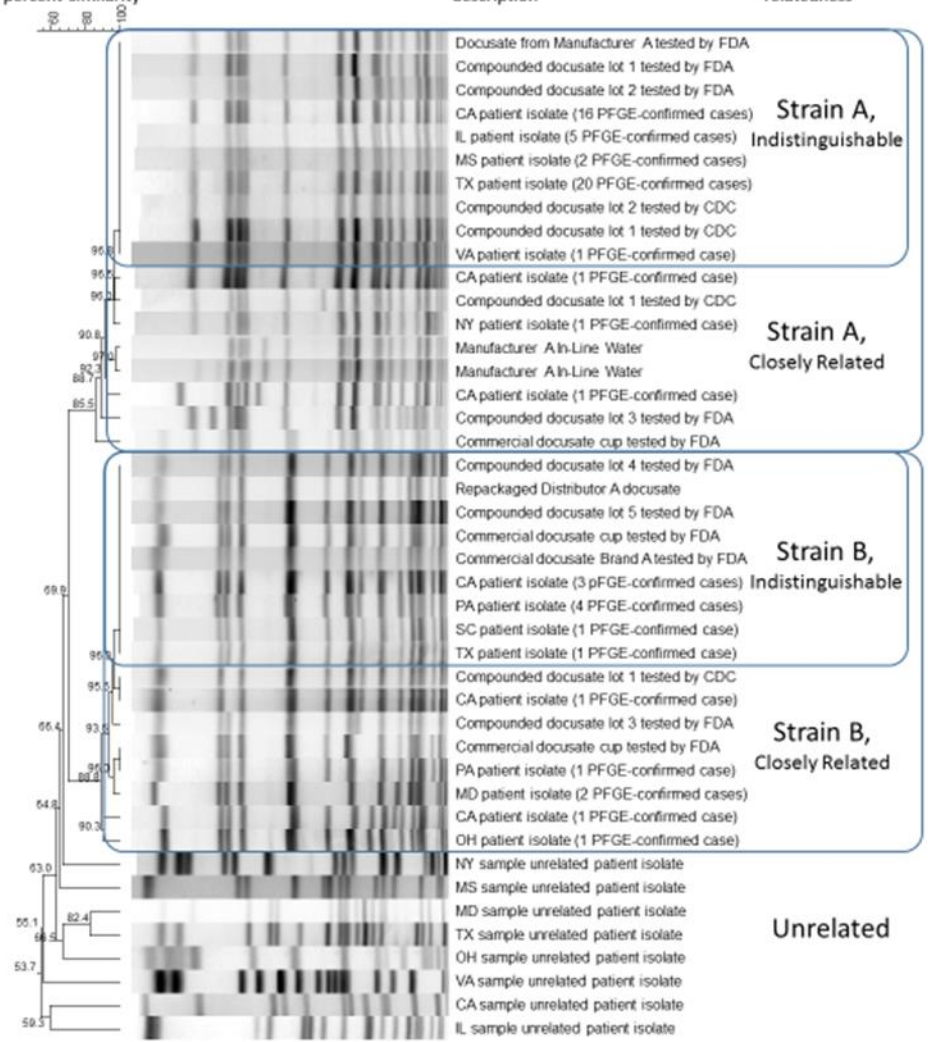
- **Confirmed: Clinical culture of Bcc indistinguishable or closely related to one of the outbreak strains by molecular typing methods collected from a patient on or after 1/1/2016.**

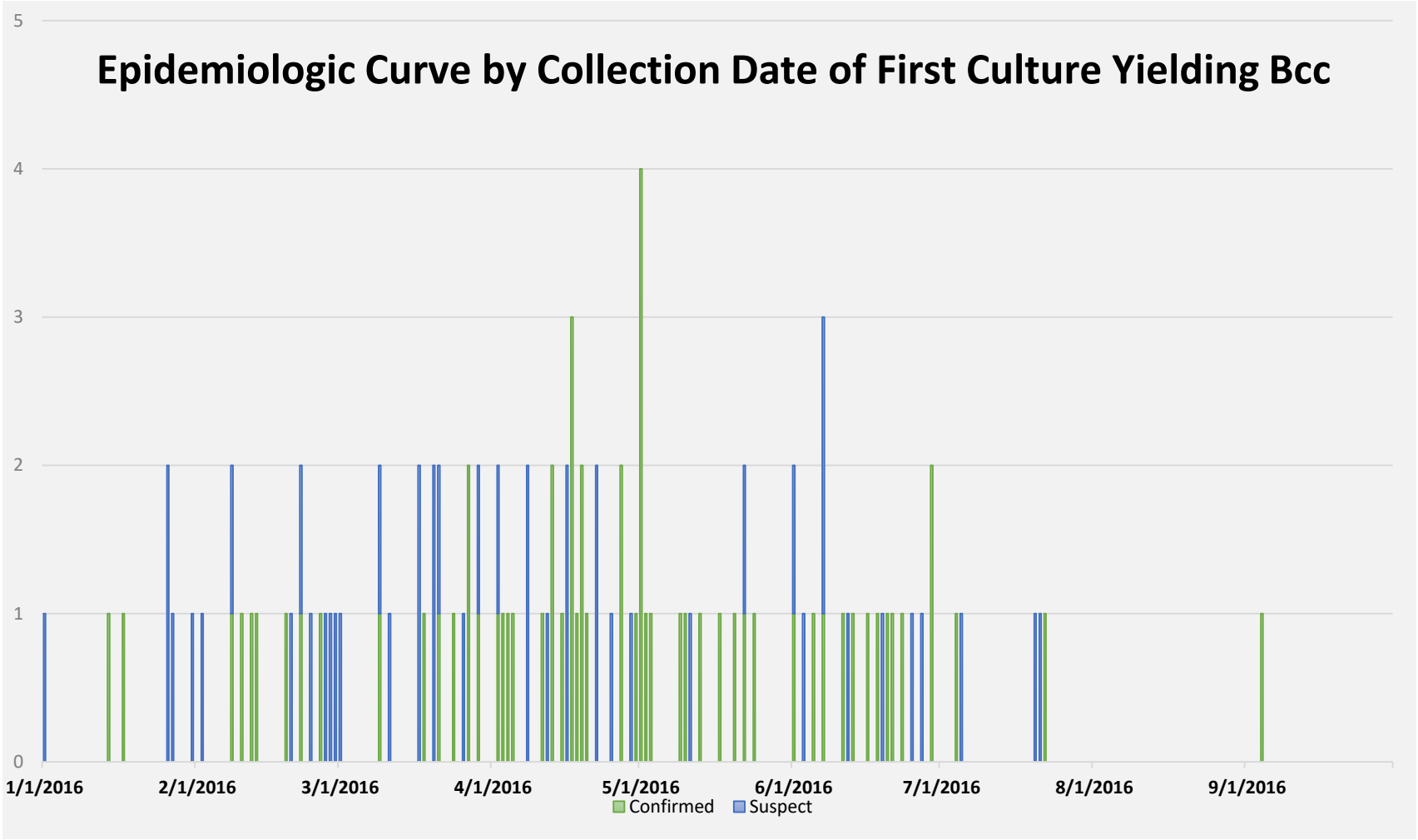
- **Suspect: Clinical culture yielding Bcc of an unknown strain type, at a facility known to have at least one confirmed case, or with known exposure to recalled liquid docusate, obtained on or after 1/1/2016.**

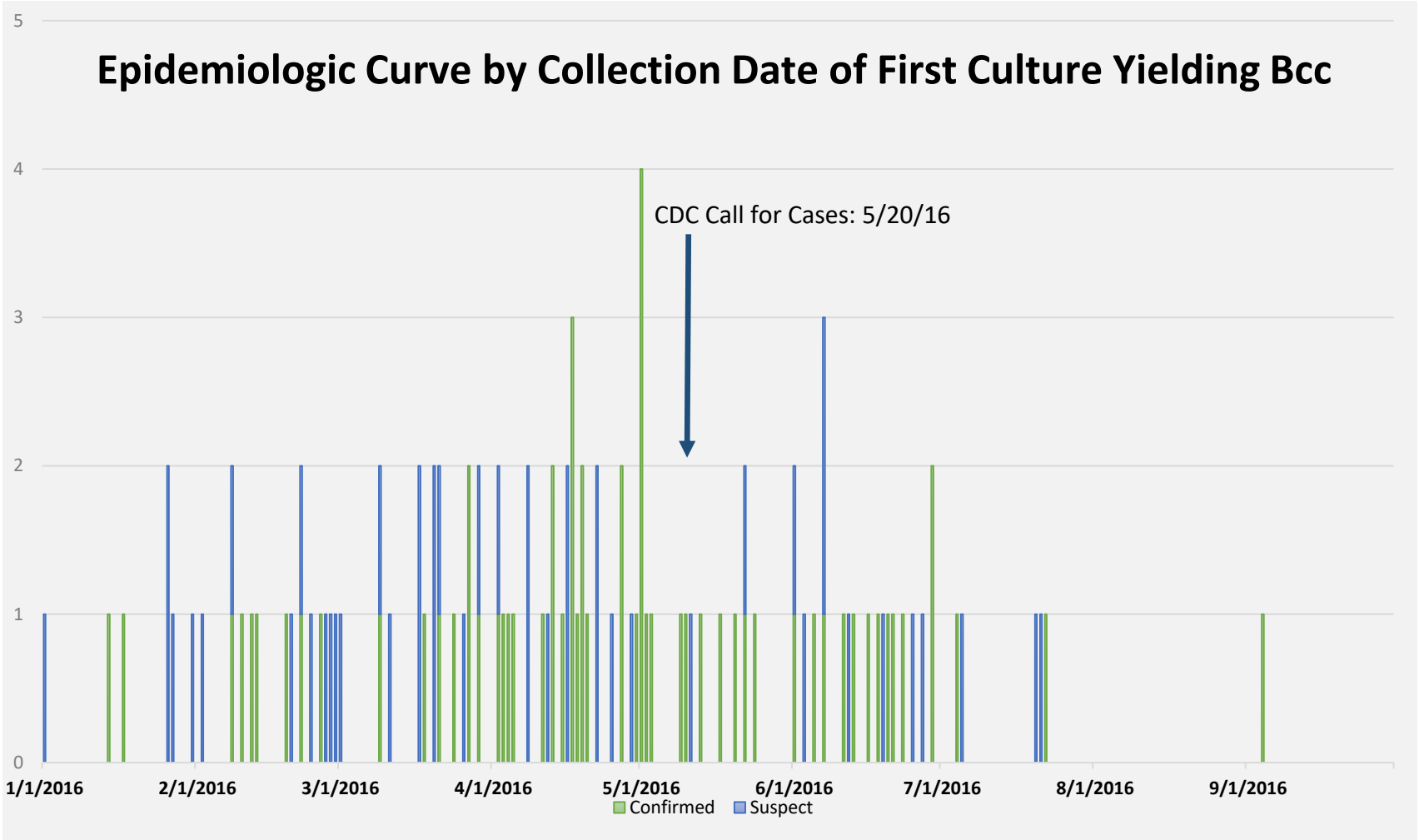
Product Recall

- FDA performed on-site inspection at PharmaTech
- Additional samples collected for culture
- FDA cultures grew Bcc from multiple lots
  - Product isolates identified which were indistinguishable from clinical isolates with Pattern A and Pattern B
  - In-line water sample from PharmaTech also tested positive for Bcc
- PharmaTech issued voluntary recall :
  - Liquid docusate products 7/14/16
  - All liquid products 8/8/16

PFGE Results




Epidemiologic Curve by Collection Date of First Culture Yielding Bcc
5
4
3
2
1
0
1/1/2016
2/1/2016
3/1/2016
4/1/2016
5/1/2016
6/1/2016
7/1/2016
8/1/2016
9/1/2016
Confirmed
Suspect


Epidemiologic Curve by Collection Date of First Culture Yielding Bcc
CDC Call for Cases: 5/20/16
5
4
3
2
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1/1/2016
2/1/2016
3/1/2016
4/1/2016
5/1/2016
6/1/2016
7/1/2016
8/1/2016
9/1/2016
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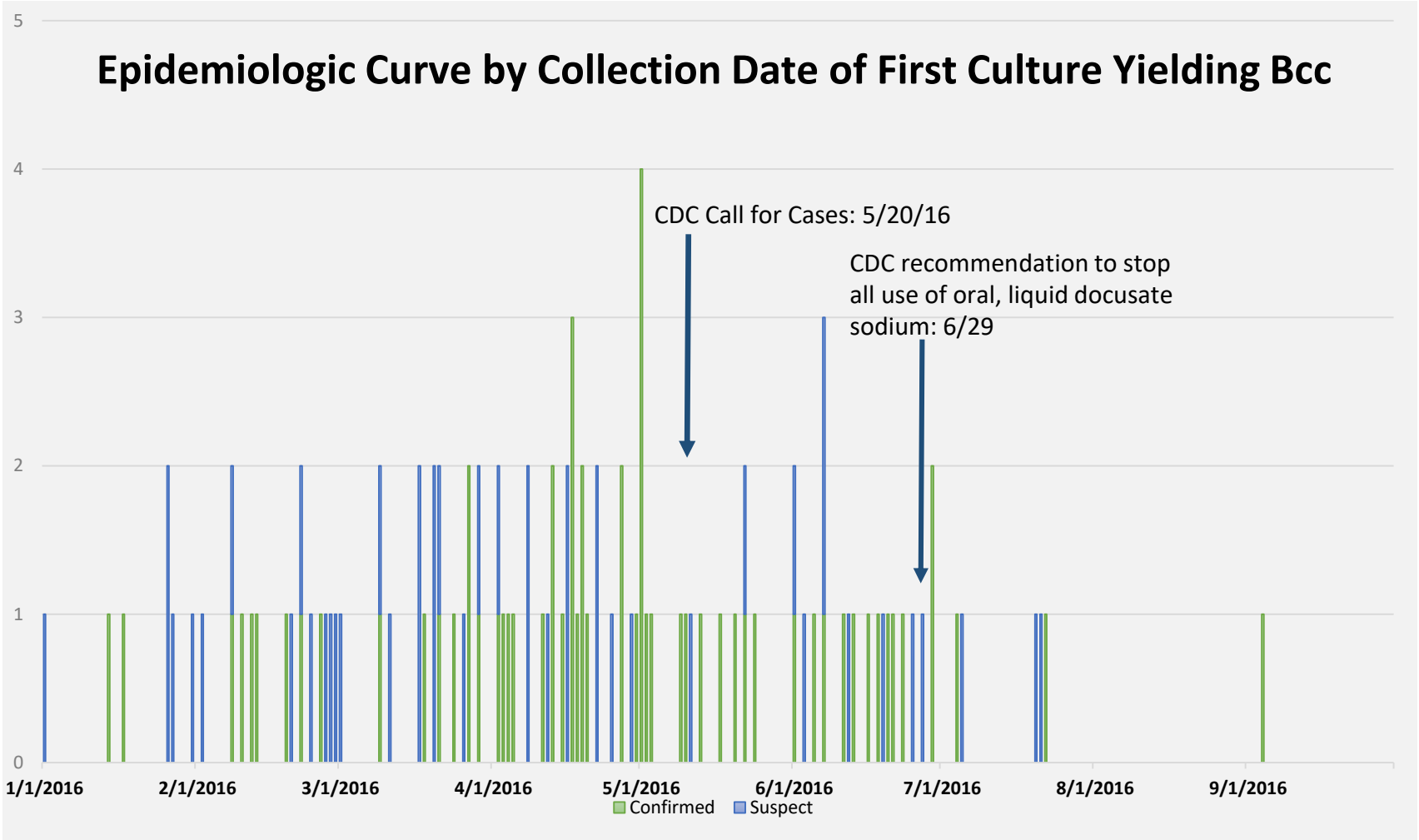
Suspect


Epidemiologic Curve by Collection Date of First Culture Yielding Bcc
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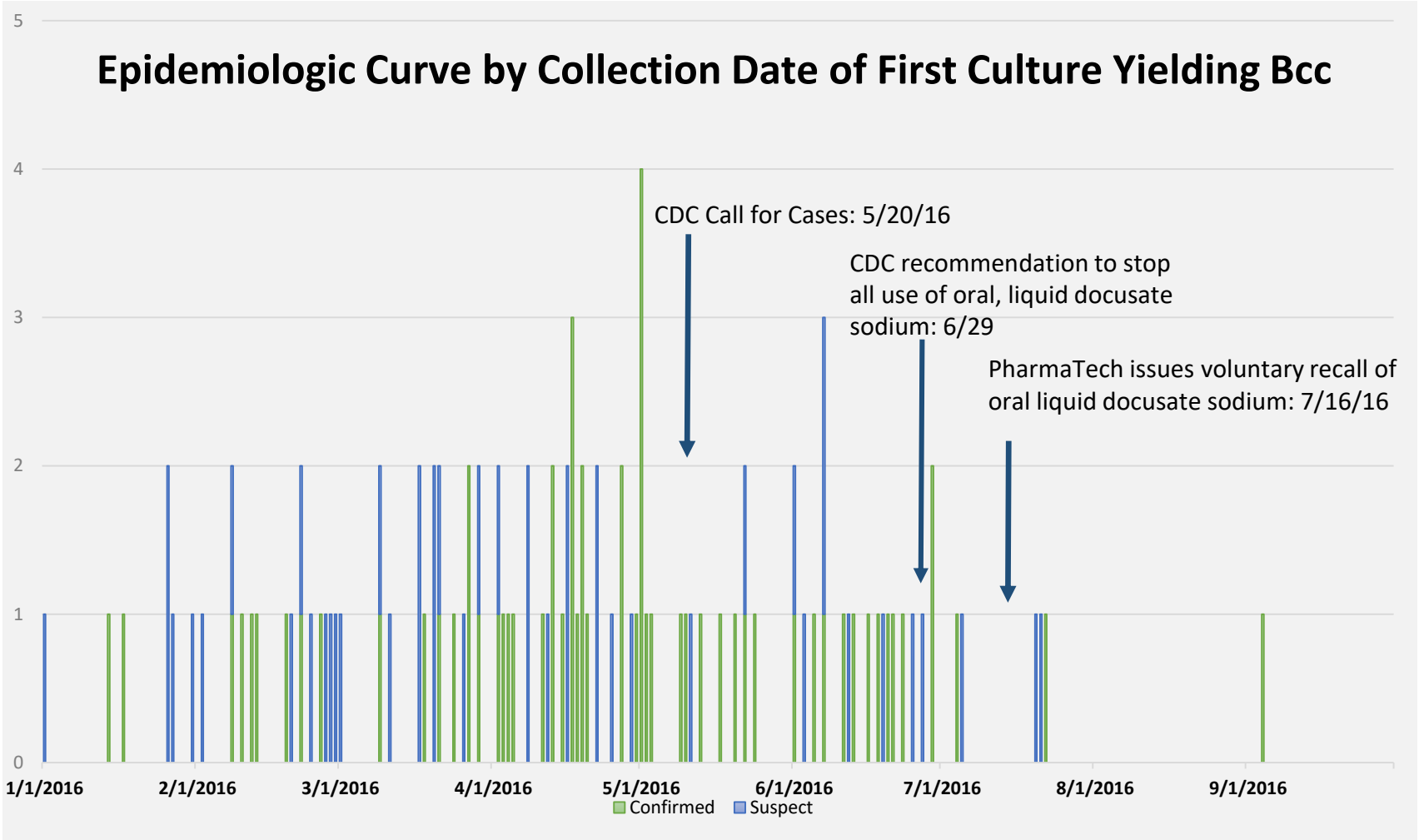
CDC Call for Cases: 5/20/16
CDC recommendation to stop all use of oral, liquid docusate sodium: 6/29
1/1/2016
2/1/2016
3/1/2016
4/1/2016
5/1/2016
6/1/2016
7/1/2016
8/1/2016
9/1/2016
Confirmed
Suspect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PharmaTech issues voluntary recall of oral liquid docusate sodium: 7/16/16
1/1/2016
2/1/2016
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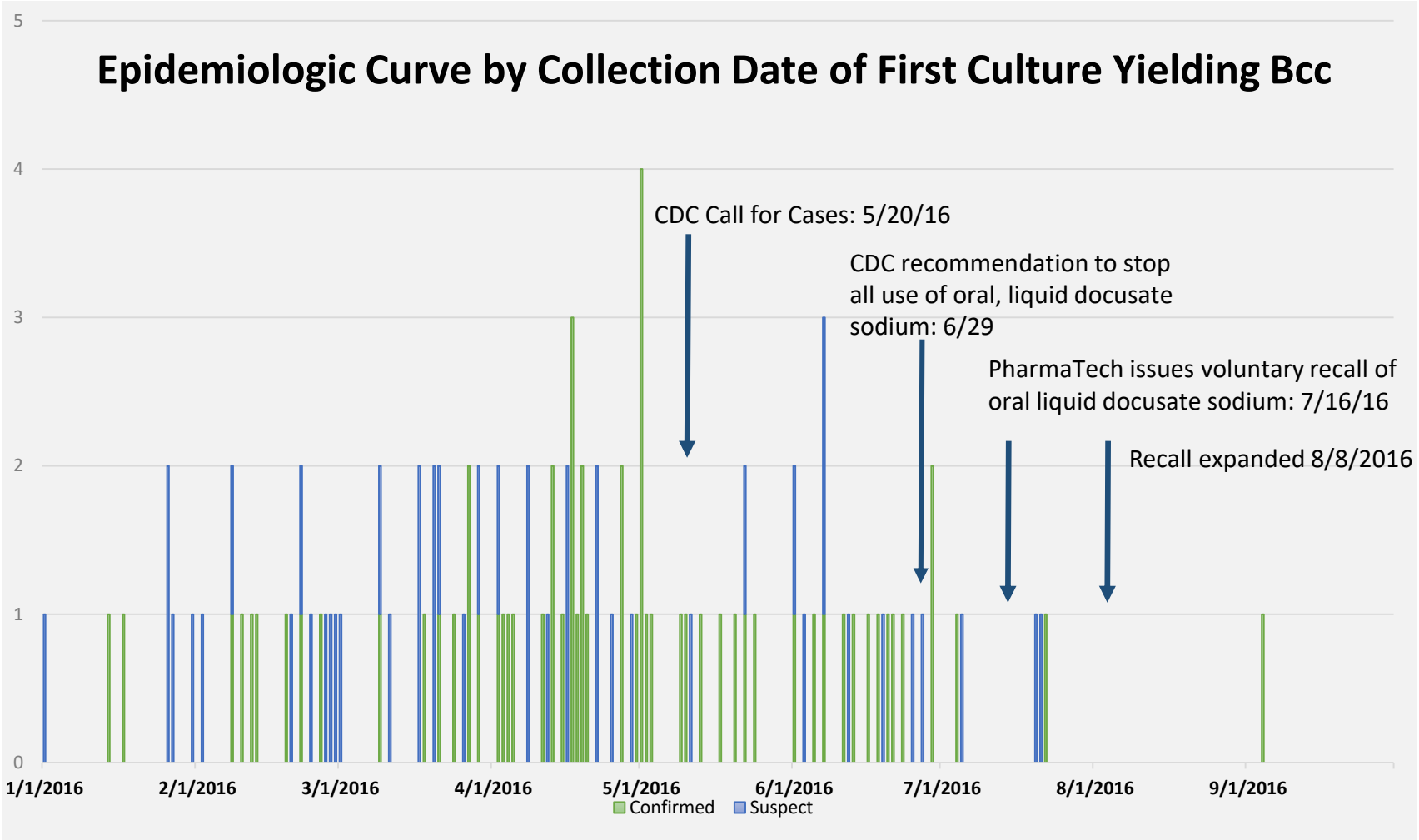
6/1/2016
7/1/2016
8/1/2016
9/1/2016
Confirmed
Suspect


Epidemiologic Curve by Collection Date of First Culture Yielding Bcc
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CDC Call for Cases: 5/20/16
CDC recommendation to stop all use of oral, liquid docusate sodium: 6/29
PharmaTech issues voluntary recall of oral liquid docusate sodium: 7/16/16
Recall expanded 8/8/2016
1/1/2016
2/1/2016
3/1/2016
4/1/2016
5/1/2016
6/1/2016
7/1/2016
8/1/2016
9/1/2016
Confirmed
Suspect

Total Cases

- Received >300 reports of positive cultures from 31 states
- CDC laboratory performed PFGE on over 100 clinical isolates
- 62 confirmed cases from 10 states
  - 48 cases indistinguishable or closely related to Pattern A
  - 14 cases indistinguishable or closely related to Pattern B
- 46 suspect cases which included 1 additional state

Outbreak #2

The Call…

- On February 16, 2018 the Pennsylvania Department of Health (PA DOH) contacted CDC to report 6 cases of Bcc infections among non-cystic fibrosis patients from an acute care hospital
  - Sites of infection included urine (1), peritoneal fluid (2), wounds (2), and sputum (1) from November 16, 2017 and January 30, 2018

The second call…

- On March 7, 2018 the California Department of Public Health contacted CDC to report 8 cases of Bcc infections urine (6), and sputum (2) from 12/26/17 to 2/12/2018 among non-cystic fibrosis patients from an acute care hospital
- On follow up PA DOH reported 4 additional patients from the same facility with urine cultures positive for Bcc

Multiple Clusters in Different States

- Initial consultations focused on infection control practices particularly near water sources
- Reports from two facilities in different states increased concern for a contaminated product
- 2nd group of cases in PA were all urine cultures as were the majority of the CA cases
- The PA DOH sent clinical isolates to the *B cepacia* reference laboratory at the University of Michigan
  - Identified the species as *B cenocepacia*
  - Clinical isolates were identical or closely related by box-PCR

Identification of a Source

- **PA hospital performed cultures on multiple common products**
  - **On March 13, reported a culture of a bottle of Remedy Essentials No Rinse Foam was positive for Bcc**
  - **The next day PA DOH collected multiple samples of the product**
  - **Eight of fifteen bottles collected positive for Bcc at state public health laboratory**

Product Investigation

- FDA notified of contaminated product
  - Product regulated as a cosmetic by FDA
  - Used for skin and perineal care for patients unable to shower or bath
- CA DPH notified of contaminated product
- Investigation by LA County DPH identified that their facility also used Remedy Essentials No Rinse Foam

Product Recall

- Samples of product in sealed boxes collected by FDA
- Samples of unused products in open boxes were sent to CDC
- Three different lots of the product were culture positive for *B cenocepacia*
- On March 28, the manufacturer issued a voluntary recall of the 3 contaminated lots

Call for Cases

March 28, 2018

EPI-X The Epidemic Information Exchange

Burkholderia cepacia complex Infections Associated with Use of Medline Remedy Essentials No-Rinse Foam -- 2018

Access and Notification:	Click to see who has viewed this report.
Distribution: Contributor's instructions for distributing this report.	**Distribute on a need-to-know basis**
Brief Summary of Report:	CDC is providing support to state and local health departments in the investigation of two clusters of Burkholderia cepacia complex (Bcc) infections at two acute care hospitals in Pennsylvania and California occurring between November 2017 and March 2018.
Description:	CDC is providing support to state and local health departments in the investigation of two clusters of *Burkholderia cepacia* complex (Bcc) infections at two acute care hospitals in Pennsylvania and California

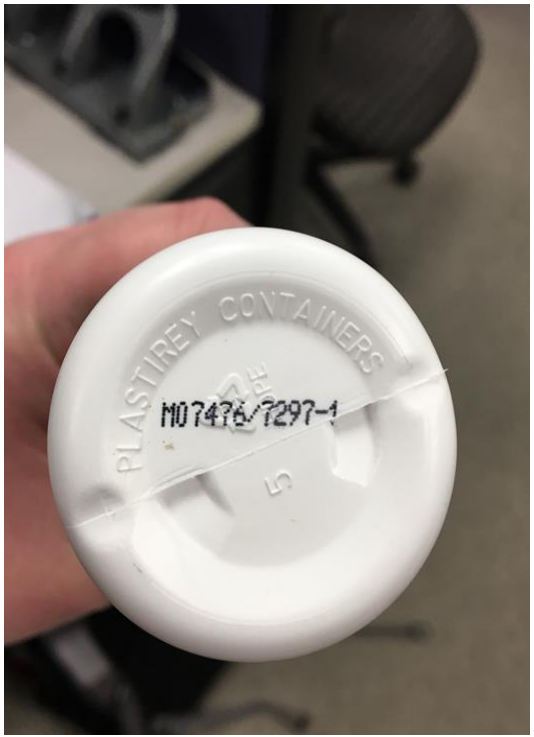
Case Definitions

- **Confirmed Case:**
  - A patient's first culture collected on or after November 1, 2017, yielding Bcc matching or closely related to an outbreak strain by molecular typing

- **Probable Case:**
  - A patient's first culture collected on or after November 1, 2017, yielding Bcc with unknown or pending strain type, and collected from a patient who received care at a facility utilizing aqueous product from a master lot manufactured at Bocchi Laboratories which has tested positive for Bcc

Exposure Data Collection

- Collected information on exposure to product and lots
  - Unable to know what lot(s) an individual patient was exposed to directly
  - Had to rely on what lots were in the facility at time of positive culture
  - Some facilities only knew what lot(s) were in the facility when they sequestered the product

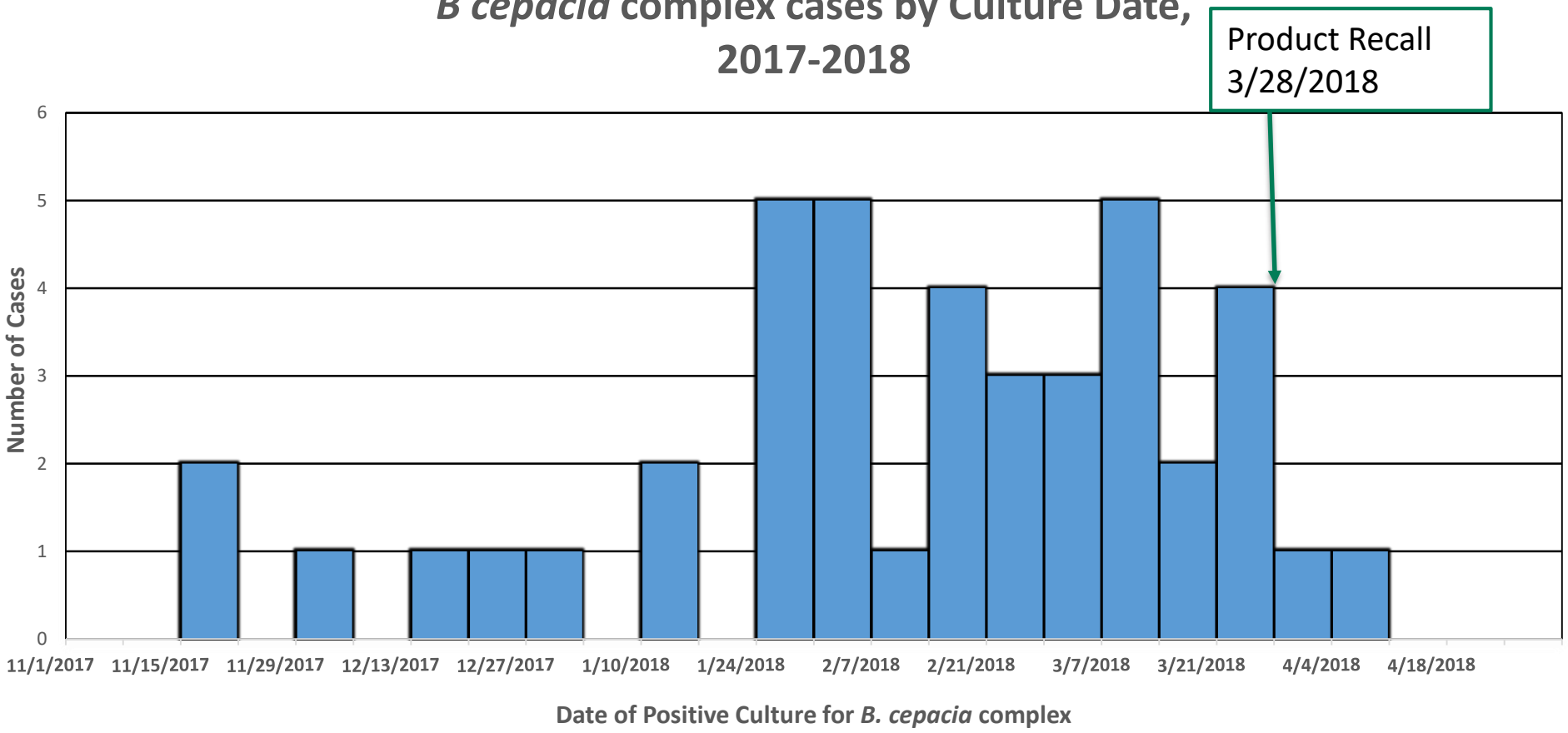


Cases and Culture Sites

- Identified 17 confirmed and 31 probable cases
- Involved 13 hospitals in 6 states

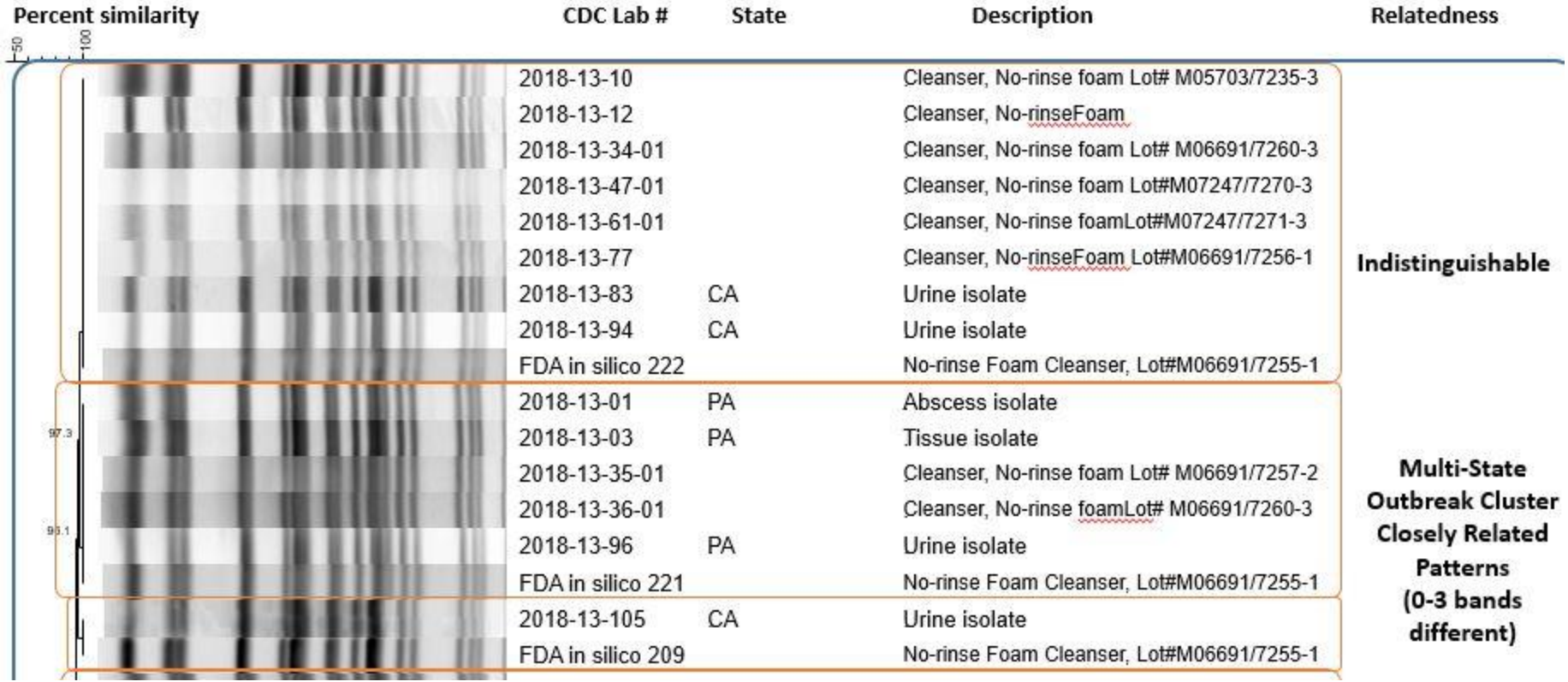
- Culture site reported for 43 of 48 cases
  - Urogenital tract – 27 (63%)
  - Respiratory tract – 9 (21%)
  - Bloodstream – 4 (9%)
  - Wound – 4 (9%)
  - Peritoneum – 3 (7%)
- Four patients had multiple positive culture sites

B cepacia complex cases by Culture Date, 2017-2018



*42 cases had culture dates available

PFGE Results



CDC Lab #	State	Description	Relatedness
2018-13-10		Cleanser, No-rinse foam Lot# M05703/7235-3	Indistinguishable
2018-13-12		Cleanser, No-rinseFoam	
2018-13-34-01		Cleanser, No-rinse foam Lot# M06691/7260-3	
2018-13-47-01		Cleanser, No-rinse foam Lot#M07247/7270-3	
2018-13-61-01		Cleanser, No-rinse foamLot#M07247/7271-3	
2018-13-77		Cleanser, No-rinseFoam Lot#M06691/7256-1	
2018-13-83	CA	Urine isolate	
2018-13-94	CA	Urine isolate	
FDA in silico 222		No-rinse Foam Cleanser, Lot#M06691/7255-1	
2018-13-01	PA	Abscess isolate	Multi-State Outbreak Cluster Closely Related Patterns (0-3 bands different)
2018-13-03	PA	Tissue isolate	
2018-13-35-01		Cleanser, No-rinse foam Lot# M06691/7257-2	
2018-13-36-01		Cleanser, No-rinse foamLot# M06691/7260-3	
2018-13-96	PA	Urine isolate	
FDA in silico 221		No-rinse Foam Cleanser, Lot#M06691/7255-1	
2018-13-105	CA	Urine isolate	
FDA in silico 209		No-rinse Foam Cleanser, Lot#M06691/7255-1	

Expanded Recall

- On May 8, 2018 manufacturer issued an expanded voluntary recall
  - Products produced on the same line as the contaminated product
  - Included an additional lot of lot of Remedy Essentials No Rinse Foam
- The site also manufactured several products regulated as over the counter medications
  - Investigated by a separate group at FDA
  - Over the counter medications were also recalled
- No additional lots or other products tested positive for Bcc at either FDA or CDC

Conclusions

- Demonstrates the importance of timely reporting of unusual clusters of illness and coordinated public health investigation
- Bcc is a problematic pathogen in healthcare due to environmental persistence and ability to contaminate aqueous solutions
- Clusters of Bcc infections in multiple facilities can suggest possible product contamination
- Contamination of aqueous medical products, including hygiene products, can lead to infections among susceptible patients
- Aqueous medical products should be considered as a potential source of Bcc outbreaks in healthcare settings

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NYS DOH
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For more information, contact CDC
1-800-CDC-INFO (232-4636)
TTY: 1-888-232-6348 www.cdc.gov

Questions?

Matthew Crist

cwu0@cdc.gov

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