

# Outbreak Investigations and Whole Genome Sequencing

Adiam Tesfai, PHD

FDA CFSAN Coordinated Outbreak Response and Evaluation

GenomeTrakr Meeting

September 27, 2018

# Outline



- Role of FDA in Foodborne Outbreak investigations
- Whole Genome Sequencing (WGS) impact on outbreak investigations ( Traditional and Retrospective )
- Examples of whole genome sequencing (WGS) in recent outbreak investigations
- Challenges and opportunities posed by WGS for foodborne outbreak investigations



# Role of FDA in Foodborne Outbreak Investigations

- FDA's role during outbreak investigations includes:
  - Traceback of suspected foods to their source
  - Food and environmental testing
  - Product and regulatory actions
  - Trace-forward (if needed)
  - Environmental assessments of farm or production facilities
  - Public communications



FDA  
**CORE**  
NETWORK | COORDINATED  
OUTBREAK  
RESPONSE &  
EVALUATION

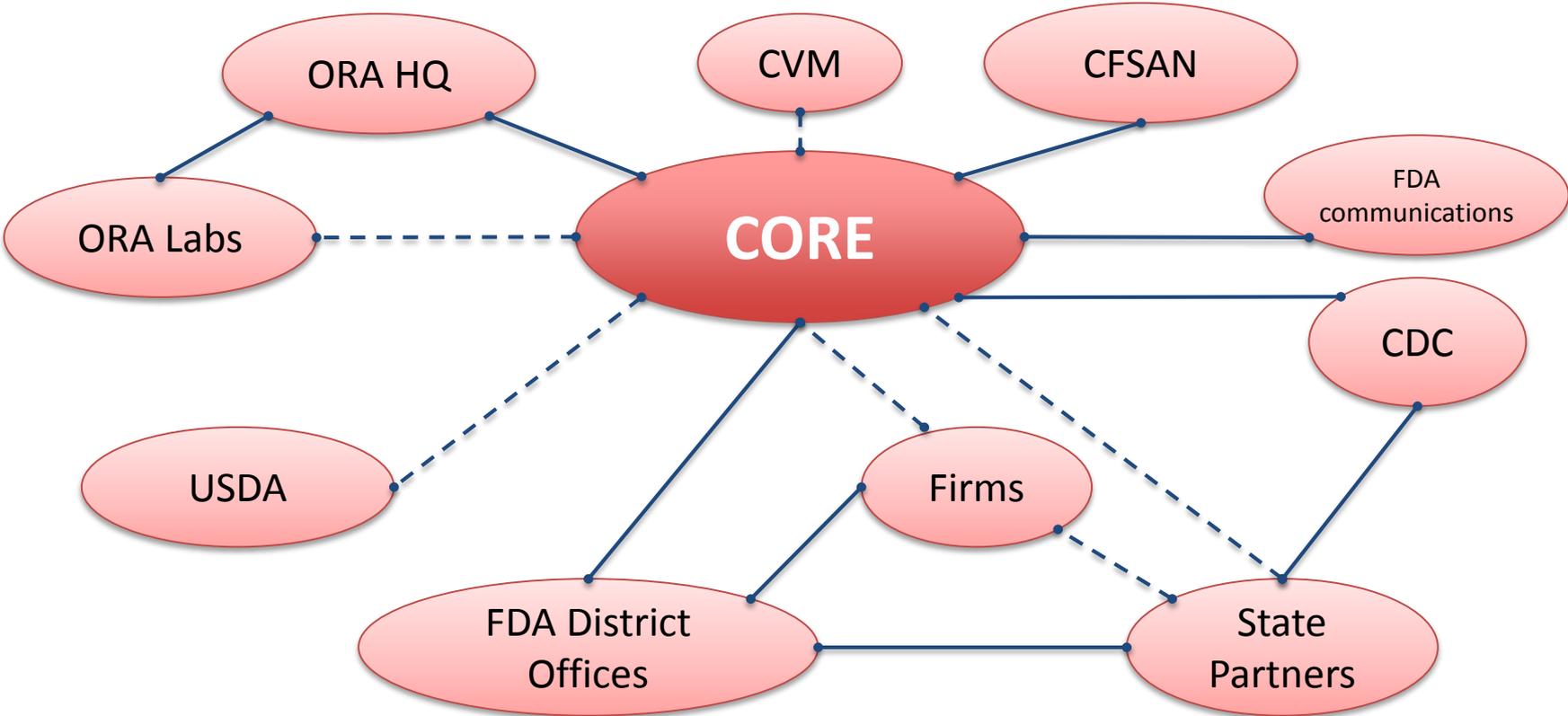


- Manages surveillance, response, and analysis activities related to incidents of illness linked to FDA-regulated human food, cosmetics, and dietary supplements
- Designed to streamline and strengthen FDA's efforts to:
  - Detect
  - Investigate
  - Respond
  - Evaluate
  - Apply Lessons Learned





# CORE Partners

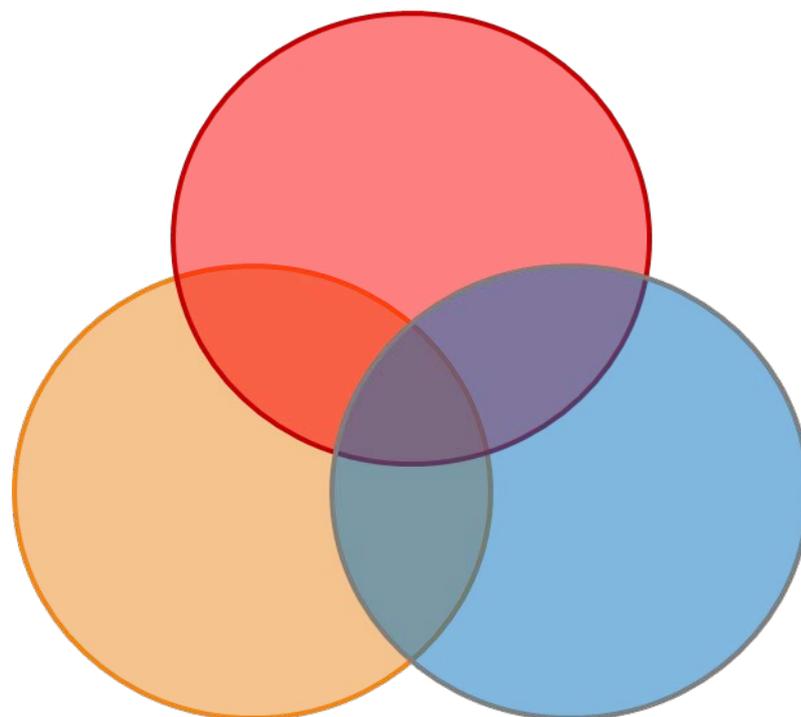


Solid lines represent lines of communication that occur for nearly every CORE outbreak; dotted lines are established for specific situations.

# Identifying an Outbreak Vehicle: Lines of Evidence

## Three types of evidence used:

- **Epidemiologic**: association between illness and food exposure
- **Traceback**: suspected food item links back to a common source of contamination
- **Microbiologic/laboratory**: pathogen found in the food, farm or facility





# How FDA uses WGS in Foodborne Outbreak Investigations



- **Traditional outbreak investigation** - FDA performs WGS on all outbreak-related samples to confirm epidemiologic links between cases and a suspect food item.
- **Retrospective outbreak investigations** - FDA uses WGS to identify links between FDA product or environmental isolates and clinical isolates (potential).
  - Compare FDA and state-generated sequences for food/environmental isolates with CDC and state-generated sequences for clinical isolates

# Outbreak of *Salmonella* Typhimurium Infections Linked to Coconut, 2018

**TRADITIONAL OUTBREAK EXAMPLE # 1**

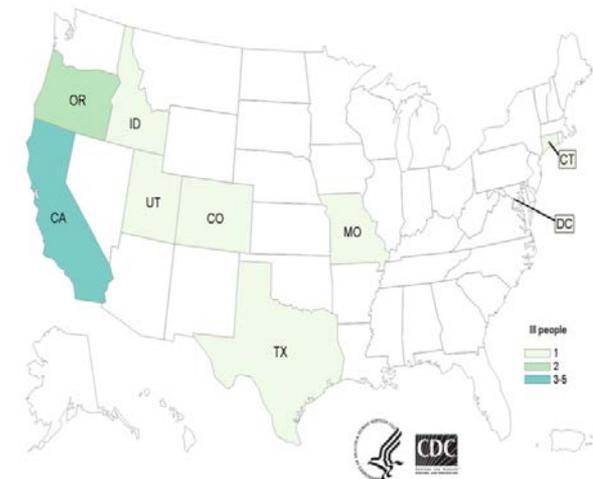


# Salmonella Typhimurium Infections Linked to Coconut, 2018



- On Jan 23, 2018, CDC notifies CORE Signals that:
  - *Salmonella* Typhimurium illnesses from six states
  - There was no definite epidemiological signal (bulk bin food products)
- States and FDA collected 23 samples from case patients home, retail outlets and distributors
- Open consumer samples of Brand A dried coconut slices revealed the presence of *Salmonella* Typhimurium

People infected with the outbreak strain of *Salmonella* Typhimurium, by state of residence, as of May 17, 2018 (n=14)





# Salmonella Typhimurium Infections Linked to Coconut, 2018

WGS assisted in confirming the vehicle from multiple leads

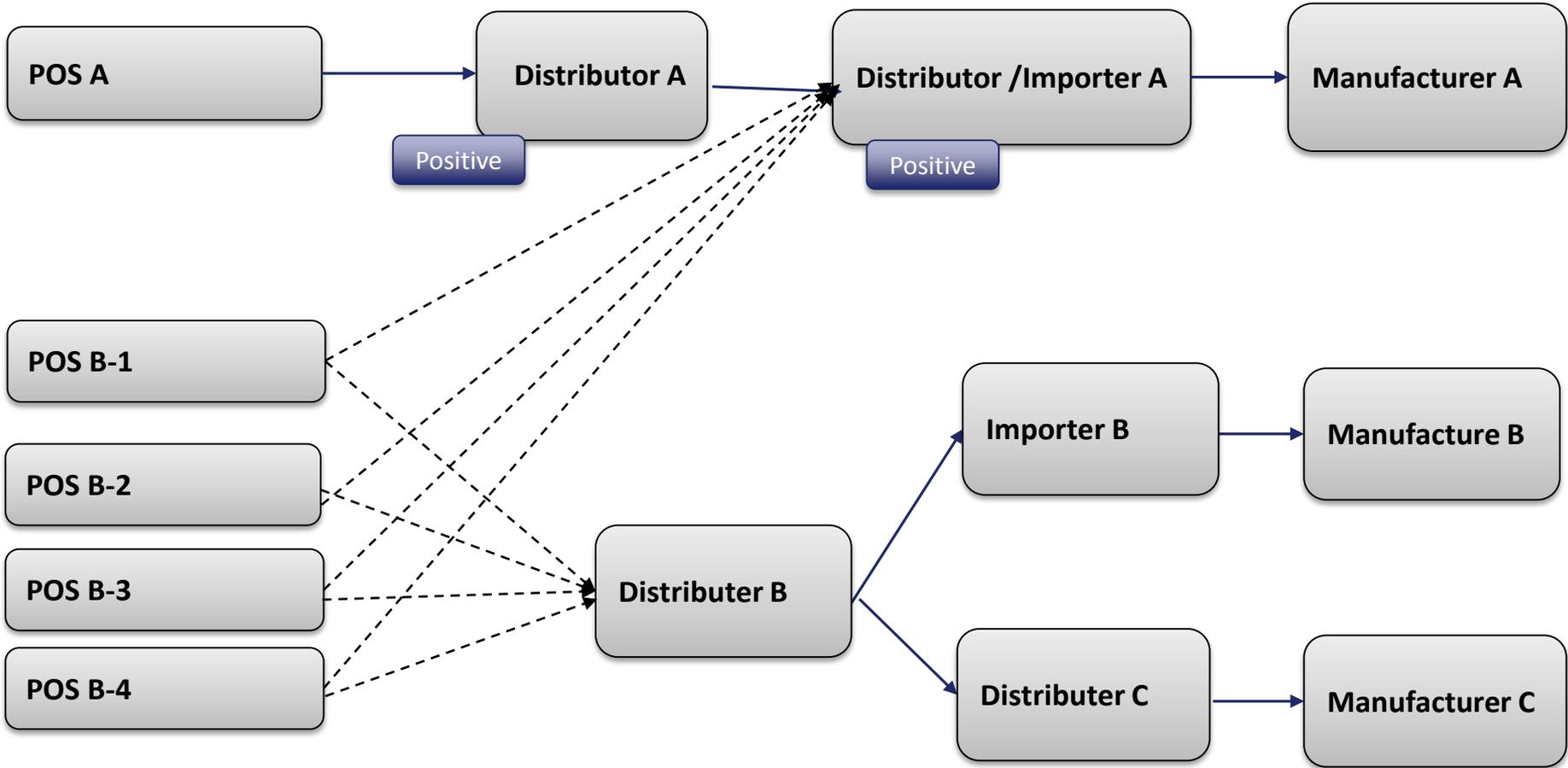
0-2 SNPs difference



- clinical, 2017-12-15, USA, PNUSAS029704, PDT000272641.2
- clinical, 2017-11-02, USA, PNUSAS026266, PDT000260320.2
- clinical, 2017-12-13, USA, stool, PNUSAS029074, PDT000270992.2
- clinical, 2017-10-27, USA, PNUSAS026498, PDT000258611.2
- clinical, 2018-02-22, USA, PNUSAS031554, PDT000288487.2
- environmental/other, 2018-03-20, USA:CO, Coconut slices, FDA00012657, PDT000296127.2
- clinical, 2018-01-19, USA, PNUSAS032039, PDT000279649.2
- clinical, 2018-03-22, USA, PNUSAS036787, PDT000297088.2
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- clinical, 2017-10-23, USA, PNUSAS023852, PDT000257051.2
- clinical, 2017-12-13, USA, PNUSAS029702, PDT000271141.2
- clinical, 2017-12-13, USA, stool, PNUSAS029789, PDT000270984.2
- clinical, 2018-01-22, USA, blood, PNUSAS032231, PDT000280601.2
- clinical, 2018-01-26, USA, PNUSAS029868, PDT000281890.2
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- environmental/other, 2018-03-20, USA:CO, Coconut slices, FDA00012660, PDT000296132.2
- environmental/other, 2018-03-22, USA:NY, Dried organic coconut, FDA00012680, PDT000297518.2
- environmental/other, 2018-03-22, USA:NY, Dried organic coconut, FDA00012681, PDT000297528.2
- clinical, 2018-03-28, USA, PNUSAS037476, PDT000300314.2
- clinical, 2018-03-28, USA, PNUSAS037122, PDT000300386.2

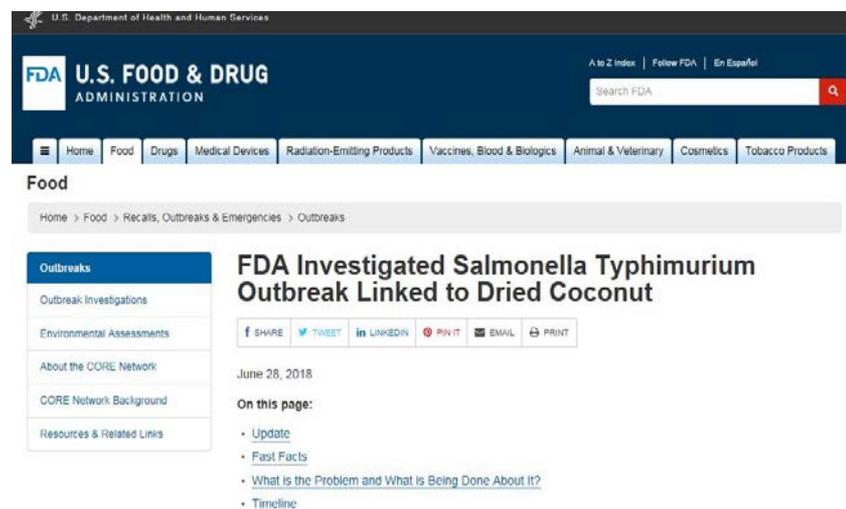


# Informational Traceback and Inspections



# Communications and Product Actions

- Outbreak posts
- Posted retail locations that received recalled bulk product
- Voluntary recall
- Import Alert



The screenshot shows the FDA website's 'Food' section. The main heading is 'FDA Investigated Salmonella Typhimurium Outbreak Linked to Dried Coconut'. The page includes a date of 'June 28, 2018' and a list of links under 'On this page': 'Update', 'Fast Facts', 'What is the Problem and What is Being Done About It?', and 'Timeline'. A sidebar on the left lists various categories like 'Outbreak Investigations', 'Environmental Assessments', and 'About the CORE Network'. The top navigation bar includes links for 'Home', 'Food', 'Drugs', 'Medical Devices', 'Radiation-Emitting Products', 'Vaccines, Blood & Biologics', 'Animal & Veterinary', 'Cosmetics', and 'Tobacco Products'.

*The U.S. Food and Drug Administration, along with the Centers for Disease Control and Prevention (CDC) and state and local partners, are investigating a multi-state outbreak of Salmonella Typhimurium illnesses that are linked to dried coconut.*

# *Salmonella* Multiple Serotypes Infections Linked to Papaya, 2017

**TRADITIONAL OUTBREAK EXAMPLE # 2**





# Salmonella Multiple Serotypes Infections Linked to Papaya, 2017

- *Salmonella* Anatum outbreak from March 2017
  - Papaya suspected as vehicle based on case exposures but TB did not converge, no sampling
- Subsequent sampling of imported papayas in August 2017 yielded a positive sample matching the old cluster by PFGE and WGS
- Confirmed papaya as the source of the outbreak AND demonstrated the contamination was an ongoing issue over multiple months



# Salmonella Multiple Serotypes Infections Linked to Papaya, 2017



**WGS contributes to further defining investigations—combining investigations/clusters**



# Outbreak of *Listeria monocytogenes* illnesses linked to ice-cream, 2015

## RETROSPECTIVE OUTBREAK EXAMPLE



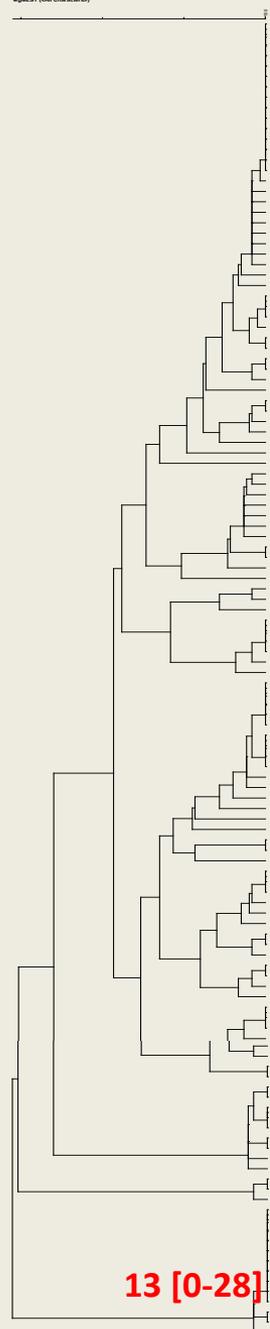
# *Listeria monocytogenes* illnesses linked to ice-cream, 2015



- Feb 2015: South Carolina found LM in Company A ice cream products (7 PFGE patterns!)
- Samples collected by Texas from production facility also found LM in “scoops” produced on same line (different PFGE pattern). PFGE of scoops sample matched 2 KS cases.
- 3 additional KS cases - occurred between Jan 2014-2015 but were different PFGE patterns than the scoops ice cream



# *Listeria monocytogenes* illnesses linked to ice-cream, 2015

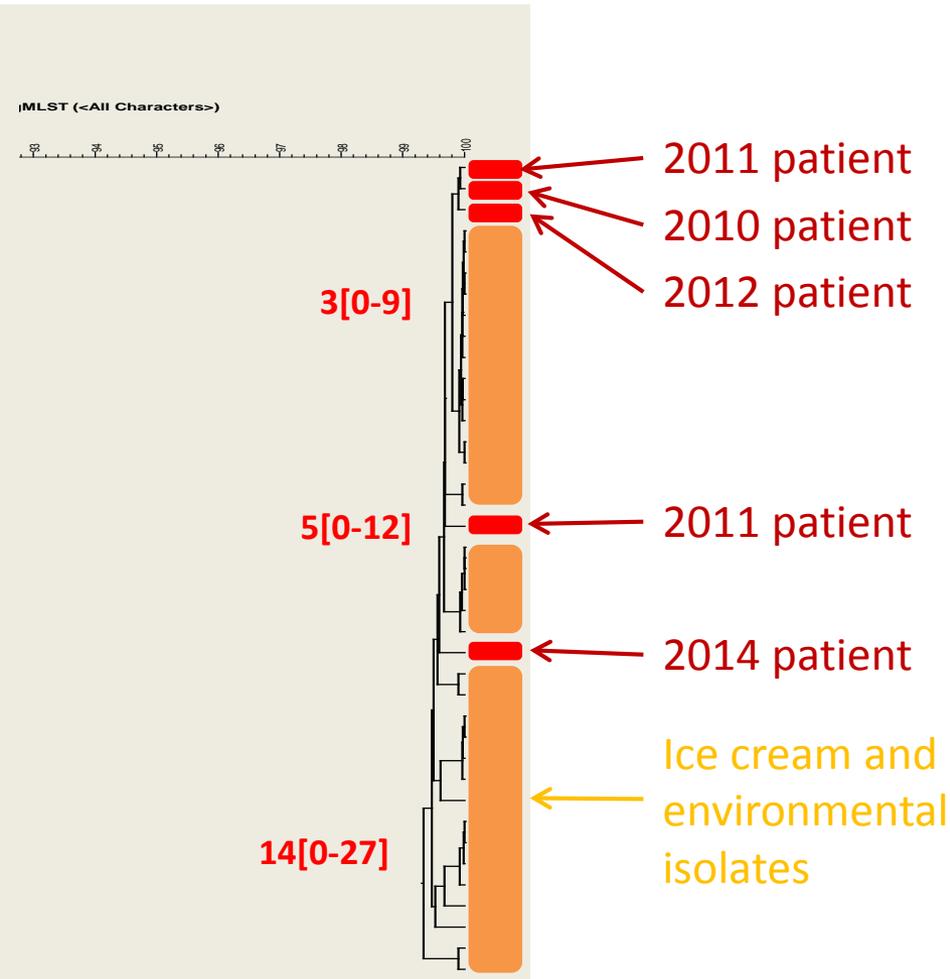


Kansas patient isolates

- CDC and KS initiate epidemiologic investigation at hospital
- April 2015: WGS shows KS patient isolates are highly related to >100 ice cream isolates from TX facility
- Epi investigation confirms 4/5 patients regularly consumed milkshakes before illness onset
- Traceback determines hospital used Company A scoops to make milkshakes

13 [0-28]

# Listeria monocytogenes illnesses linked to ice-cream, 2015



- Additional product samples from Company A Oklahoma facility were highly related to five additional cases
- Company A subsequently initiated nationwide recall (all products, all production facilities) on April 21, 2015
- Production halted in multiple facilities, corrective actions initiated



# Advantages/Challenges of WGS

- Greater confidence in isolate relatedness
  - Breaks PFGE clusters apart, brings together different patterns
- Use of WGS for foodborne outbreak detection and response can result in:
  - Identification of more clusters, smaller case counts
  - Shift in temporal boundaries of an outbreak
  - Improved targeting of resources
  - Enhanced foodborne illness attribution



# Advantages/Challenges of WGS

- Integration: Transition from PFGE to WGS in current outbreak detection and response platforms and procedures
- Interpretation: How close is close enough? What does relatedness mean?
- Communication: How do we communicate WGS results to different audiences (firms, lawyers, publicly)?

## Acknowledgements

- CDC/National Center for Emerging and Zoonotic Infectious Diseases
  - Outbreak Response & Prevention Branch and Enteric Diseases Laboratory Branch/Division of Foodborne, Waterborne and Environmental Diseases
- FDA/Center for Food Safety and Applied Nutrition
  - Division of Microbiology/Office of Regulatory Science
  - Office of Analytics and Outreach
  - Coordinated Outbreak Response and Evaluation (CORE) Network-especially Jenifer Beal
- All other investigation partners

