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# Food & Beverage Industry Perspective on WGS FSIS Public Meeting

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# Who is “food and beverage”



American Bakers Association



• NMPF

• National Pork Producers Council

• Natl Rest Assn

• NCA

• NTF

• NHC

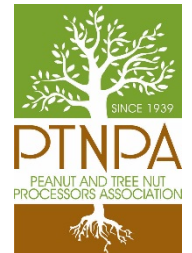
• NWFFPA

• OFW Law

• PMA

• SFA

• Western Growers



• NAMI

• NCC

# Root of the Concern

- What industry heard a few years ago

WGS is the greatest thing ever (and we won't need epi anymore).

WGS match between a food and clinical isolate **doesn't** mean food caused illness. Epi and traceback critical

Present Day, CDC

## Fear of warning letters

“The WGS phylogenetic analysis of these five (5) isolates finds that they comprise two (2) strains of *L. monocytogenes*. **Comparing** these five (5) strains to the larger **WGS database** shows that four (4) of the isolates are virtually identical to twenty eight (28) isolates from sample [abc] and [xyz] collected in January of 2016 from the same facility. This demonstrates a **resident strain** of *L. monocytogenes* has maintained its presence in your facility since at least January of 2016. The presence of a resident strain of *L. monocytogenes* in your facility is significant in that it demonstrates your sanitation efforts are inadequate to effectively control pathogens in your facility to **prevent contamination of food.**”



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Voluntary Recall 07/19/2014



(WGS) analysis by whole-genome multilocus sequence typing showed that isolates cultured from the Massachusetts and Minnesota patients were highly related (<10 allele differences and <10 high-quality single nucleotide polymorphism differences) to the isolates from recalled fruits

9  
illnesses  
over 2.5  
yrs

WGS showed that the *Listeria monocytogenes* isolated from the frozen corn was closely related genetically to eight bacterial isolates from ill people... This close genetic relationship provides additional evidence that the people in this outbreak became ill from eating frozen vegetables produced by CRF Frozen Foods. ...environmental samples collected by FDA from Oregon Potato Company, located in Pasco, WA, were found to be closely related genetically to eight of the isolates of ill people associated with this outbreak.

# Request for Public Meeting

- Equivalency of methods between regulatory and public health agencies
  - FDA’s use of SNPs and CDC’s use of WgMLST-based approach
- Plans to “sunset” PFGE and prerequisites for reliance on WGS?
- Compliance policy guide to govern the use of WGS
- How is epidemiological and traceback information used in conjunction with WGS during an outbreak investigation?

- Retrospective analyses and potential future regulatory action
- Collaboration with local, state, or other federal agencies or programs, *e.g.*, NARMS, on WGS activities?
- International standards around WGS (*e.g.*, within Codex Alimentarius)?
- Flow of WG sequence information to different databases (*e.g.*, what governs whether a sequence will be uploaded to GenomeTrakr, PulseNet etc.?)

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# Discussions to Date

- IFSH
- Individual meetings
  
- Main topics
  - Science (methods, interpretation etc.)
  - Regulatory use
  - Consistency and alignment between public health and regulatory agencies



# Concerns

- Communication of information- Day 1

FDA's laboratory analysis of the environmental samples collected during our 2017 inspection, confirmed that two (2) environmental swabs were positive for *L. monocytogenes*. Specifically, these positive samples were taken from the Production Line 6 left, conveyor bearing at end of Section 3, which is an area adjacent to a food contact surface, and a floor drain. Furthermore, this was not the first time FDA investigators collected environmental samples from your facility that were found to be positive for *L. monocytogenes*. Environmental swabs collected during our 2015 inspection revealed *L. monocytogenes* in three (3) locations within your facility and environmental swabs collected during our 2013 inspection revealed *L. monocytogenes* in three (3) locations within your facility.

The referenced environmental samples were furthered analyzed using Whole Genome Sequencing (WGS). WGS analysis of bacterial human pathogens provides high-resolution data, enabling direct links to be established between clinical isolates and food or environmental sources of bacterial contamination and illness. WGS data can also be used to infer the evolutionary relationships (or phylogeny) within a given set of isolates as it measures each DNA position in a bacterial genome. WGS analysis finds that there are resident strains of *L. monocytogenes* within your facility.

- Day 21: “As requested, I have attached the samples which have been analyzed and found to be positive for *Listeria monocytogenes*. The WGS data will be provided at our meeting. It requires clearance and is being processed.”
- Day 34: “Late yesterday afternoon I received the WGS report. The tree doesn’t include the verbal analysis, which is really the most useful information. Analyzing and interpreting these trees are delegated to our Experts, to avoid misinterpretation. CFSAN experts will further explain the analysis during the meeting.”
- (meeting occurred at 56 days)

# What should be communicated?

- Science & Protocols → Actionable Info
- Where were the pathogen sample positives found (e.g. Lm found)?
- In what zones were the pathogen sample positives found?
- What dates were the pathogen sample positives found?
- Has any product from this facility and specifically this production line tested positive for this pathogen?

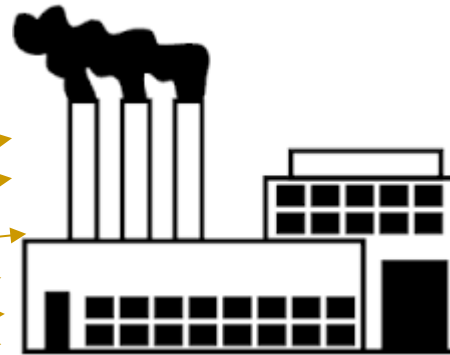
# Regulatory questions

- Access to the analytical packet (test methods used, results, chain of custody, what is the lab positive control strain)?
  - At what point is this “evidence”?
- Via WGS, how closely related are each of the sample positives?
  - Method to determine differences?
  - What is the reference strain for determining relatedness?

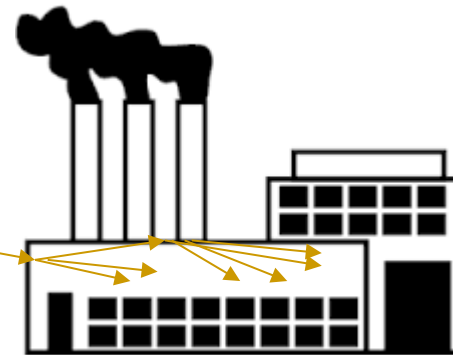
# Result interpretation

- Have any of these WGS strains been associated with human illnesses?
  - If there is a report, what is the associated meta data?
- This could be a repeat transient Lm introduction from a repeatedly used farm/supplier.
  - Have post sanitation environmental monitoring *Listeria spp* test results been generated to determine if this is a true resident Lm issue?

# Resident or Repeat Transient?



Resident in orchard, transient in facility



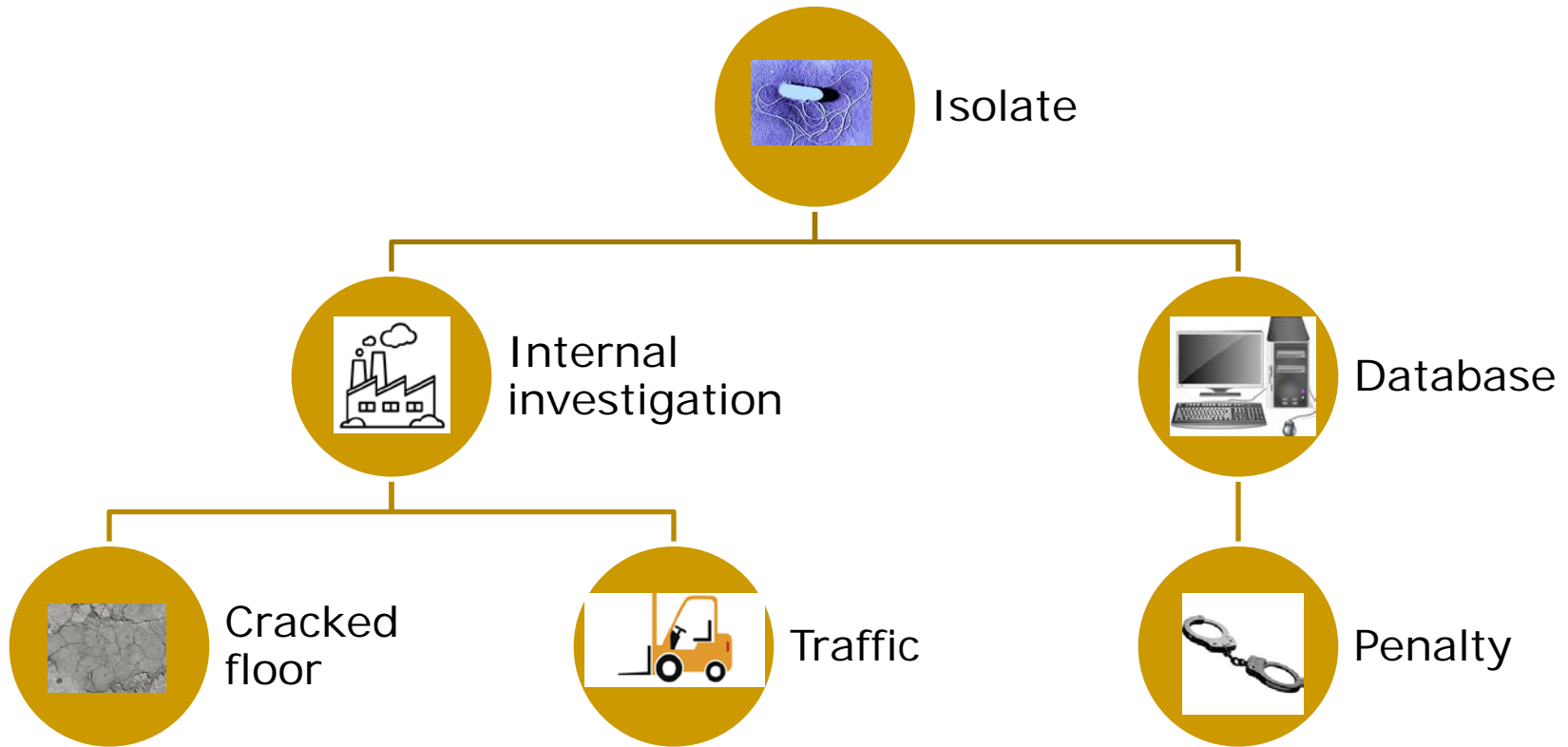
Resident in facility

-what is the true ubiquity of sequences?

# Policy Alignment

- NARMS program, State public health groups, Department of Homeland Security research projects...Many groups are doing WGS for different reasons
  - How do they communicate with each other?
  - What is the process for regulatory agencies once notified of the findings?
  - How do they interact with industry?
    - Communication of information
    - Regulatory action

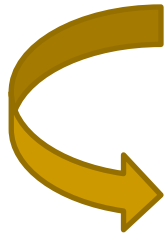
# Should Industry do WGS?





# Retrospective Investigations

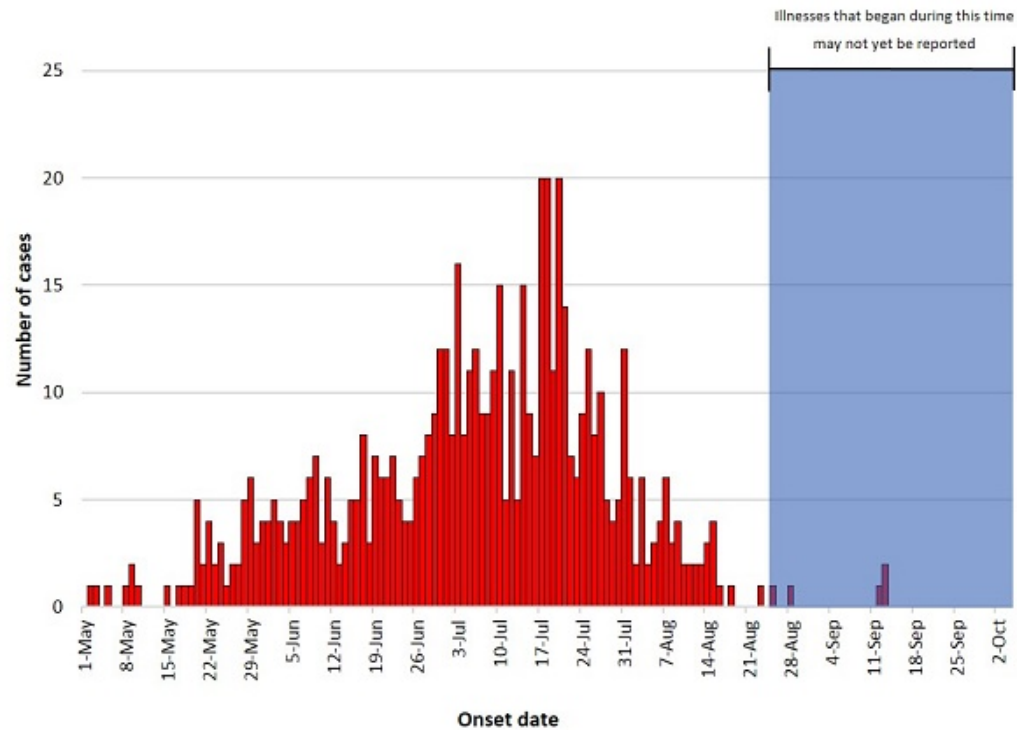
- If you collect WGS data must you share it?
  - Are blinded data really safe?
  - Metadata: friend or foe?
- Once in the database it's there forever
- What do we know about ubiquity, genetic drift?



Role of epi, traceback,  
etc.

# Opportunities

- 592 *Cyclospora* cases *not* associated with foreign travel



# Summary

- WGS is here to stay
  - High fidelity method
  - Still gathering more data & understanding how to interpret it
- Outstanding questions
  - Role in an investigation
  - Approach to one-off illness
  - Quantitative methods
    - Live/dead; dose response; gene expression/virulence
  - Retrospective analyses
  - What guides regulatory use of WGS?

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# Questions?

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