Control of *Listeria monocytogenes* in Ready-to-Eat Foods: Draft Guidance

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Introduction
Lm Time Points

• “Zero tolerance” established by FDA and USDA in 1986. Published in 1996 *Food Control* journal
• 2003 FDA/FSIS risk assessment
• 2004 FAO/WHO risk assessment
• 2008 FDA draft guidance documents
• 2011 JIFSAN-IRAC workshop on dose-response
• Notable outbreaks (produce and dairy)
• Ice cream prevalence and enumeration studies
• 2015 dose-response study
• 2015 FDA Food Advisory Committee meeting
• 2017 FDA new draft guidance document
Key Point from 2015 FAC Meeting

Based on knowledge gained from recent outbreaks (e.g., ice cream) and the 2015 dose-response evaluation, FDA remains uncertain that the 100/gram standard for foods that do not support growth provides an appropriate level of protection for the most vulnerable individuals in the at-risk subpopulations.
Ice Cream Prevalence and Enumeration Results

Samples were from seven lots produced in November 2014, December 2014, January 2015, and March 2015.

*L. monocytogenes* detected in 99% (2,307 of 2,320) of samples

Geometric mean per lot of *L. monocytogenes* in these samples: 0.15 to 7.1 MPN/g.
Estimated Number of Listeriosis Cases by Dose of *Listeria monocytogenes* from FDA 2015 Dose-Response Study

<table>
<thead>
<tr>
<th>Dose of Lm</th>
<th>Dose Log$_{10}$</th>
<th>No. cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>3</td>
<td>0.5</td>
<td>0</td>
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<tr>
<td>10</td>
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<td>1</td>
</tr>
<tr>
<td>32</td>
<td>1.5</td>
<td>1</td>
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<tr>
<td>100</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>316</td>
<td>2.5</td>
<td>3</td>
</tr>
<tr>
<td>1,000</td>
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<td>6</td>
</tr>
<tr>
<td>3,160</td>
<td>3.5</td>
<td>14</td>
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<tr>
<td>31,600</td>
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<td>100,000</td>
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</tr>
<tr>
<td>1,000,000</td>
<td>6</td>
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</tr>
</tbody>
</table>

* Pouillot et al. 2015. Table III. *Risk Analysis* 35(1):100
Control of *Listeria monocytogenes* in Ready-to-Eat Foods: Draft Guidance

- **Federal Register** / Vol. 82, No. 10 / Tuesday, January 17, 2017
Applicability

• Guidance intended for those subject to the CGMP & PC rule in 21 CFR part 117.

• Applies to production of RTE foods exposed to the environment prior to packaging where there is no Lm control measure that would significantly minimize Lm

• Replaces the previous draft guidance from 2008
Disclaimer

• The revised draft guidance, when finalized, will represent the current thinking of FDA on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternate approach if it satisfies the requirements of the applicable statutes and regulations.
Background

- *Listeria monocytogenes* (Lm) in foods can cause listericidal gastroenteritis and a severe, invasive illness (listeriosis) with a relatively high mortality rate.
- Persons at greatest risk: pregnant women and their fetuses, the elderly, and persons with weakened immune systems.
- Foods that have caused outbreaks are typically ready-to-eat (RTE) foods contaminated from the environment during manufacturing/processing.
- The greatest risk for listeriosis is from RTE foods that support growth of Lm.
Controls

• Controls on personnel
• Design, construction and operation of the plant
• Sanitation
• Controls on raw materials and other ingredients
• Listeristatic formulation controls
• Listericidal process controls
• Storage practices, time/temperature controls
• Transportation
Goal of an Environmental Monitoring (EM) Program

• Verify the effectiveness of control programs for Lm;
• Find Lm and harborage sites if present in a plant; and
• Ensure that corrective actions have eliminated Lm and harborage sites when found in a plant.
Well-Designed EM Program

• Should include
  – Collecting environmental samples from food contact surfaces (FCSs) and non-FCSs in a plant;
  – Testing the collected environmental samples to identify potential sources of contamination; and
  – Taking appropriate corrective actions if test results indicate the presence of *Listeria* spp. or *L. monocytogenes* in an environmental sample.
More on Design of the EM Program

• The guidance recommends testing for *Listeria* spp. to correct situations that could potentially lead to contamination with Lm.

• The guidance recommends testing both FCSs and non-FCSs at each sampling time.

• The guidance recommends collecting environmental samples at a time several hours into production and preferably just before cleanup.

• The guidance acknowledges that finding *Listeria* spp. is expected.
Risk-Based Corrective Action Procedures

• Consider:
  – Whether the environmental contamination is on an FCS or a non-FCS;
  – Whether testing environmental samples results in an isolated positive result or multiple positive results; and
  – The proximity of a contaminated non-FCS to FCSs.
Corrective Action Procedures

• Types of corrective actions are highly varied, depending on the situation but include:
  – conducting intensified cleaning and sanitizing,
  – conducting intensified sampling and testing,
  – conducting a root cause analysis, and
  – implementing "hold and test" procedures.

• Examples are provided; it is not possible to provide a comprehensive set of corrective actions that apply in all situations.
Escalating Actions Based on Risk

• If *Listeria* spp. is found during routine sampling:
  – Clean and sanitize the area with the positive
  – Retest during subsequent production cycles
  – Conduct comprehensive investigation if FCS
  – Return to routine testing if follow up (retest) samples are negative

• If follow up testing shows a second positive:
  – Conduct intensified cleaning and sanitizing (with disassembly if positive FCS)
  – Conduct intensified sampling and testing
  – Begin “hold and test” if FCS positive and product supports growth (consider for no-growth food)
  – Conduct comprehensive investigation
Corrective Actions for *Listeria* spp. on an FCS

- Guidance describes corrective action procedures that differ based on whether a food supports growth of Lm or not.
- Guidance recommends that for foods that do not support growth, but that are specifically intended for establishments such as hospitals and nursing homes, the corrective actions for foods that support growth be applied.

Continued
Corrective Actions for *Listeria* spp. on an FCS (cont.)

- Guidance describes corrective action procedures that specify 3 consecutive days of negative tests before returning to routine sampling and testing.

- Guidance recommends that if follow up testing results in a 3rd FCS-positive for foods that support growth, production be stopped pending consultation with food safety experts.
Comprehensive Investigation for an FCS-Positive

- Examine equipment and area surrounding positive for potential harborage sites
- Review HACCP/Food Safety Plan and its implementation
- Conduct intensive sampling and testing, collecting samples several times during production and testing upstream from the positive site

Continued
Comprehensive Investigation for FCS-Positive (cont.)

• Check maintenance records
• Interview and observe sanitation, maintenance, and production personnel
• Review production, maintenance, and sanitation procedures
• Review traffic patterns, equipment layout, and adherence to personnel hygiene procedures
Sampling and Testing Foods

- Could be done to verify supplier control programs
- Could be done for “hold and test” during corrective actions
- Could be done to verify adequacy of Lm controls for an RTE food
- Could be done to satisfy customer request/requirement

Continued
Sampling and Testing Foods (cont.)

• Guidance recommends that foods be tested for Lm rather than *Listeria* spp.

• Guidance recommends holding product represented by the food tested (e.g., food lots produced from cleanup to cleanup)
Corrective Actions for Detection of Lm in RTE food

- Reprocess with a validated listericidal control measure,
- Divert to a use in which the food will not be consumed by humans or animals,
- Send for use in food to be consumed by animals where appropriate, or
- Destroy the lot(s) of RTE food in which *L. monocytogenes* has been detected
Corrective Actions for Detection of Lm in RTE food (cont.)

- Determine whether other lot(s) of food are potentially contaminated with Lm and segregate and hold those lots of food.
- Conduct intensified sampling and testing of FCSs and non-FCSs followed by corrective actions until source of contamination is found and eliminated.
- Determine whether any food in commerce would be subject to a recall.
Analysis of Data for Trends

• Guidance recommends analyzing the data collected through environmental monitoring over time for trends that can help to continuously improve sanitation conditions in the plant by reducing the percentage of overall positive environmental samples in the plant.

• Guidance recommends analyzing product testing data for trends to improve performance and identify the need for corrective actions.
Trends in EM Indicating Lm is Not Being Controlled

- Increases in positive environmental samples in particular sites or areas;
- Finding *Listeria* in the same area on multiple but non-consecutive sampling occasions (e.g., positive one week and negative the next, appearing to be isolated positives); and
- An increase in the percentage of overall positive environmental samples in the plant.
Training

• Guidance recommends providing training in health and hygienic practices specific to control of Lm for all personnel and contractors who enter production and storage areas (e.g., individuals who conduct production, maintenance, quality assurance, quality control, or warehousing operations).
Please Submit Comments

- Federal eRulemaking Portal: https://www.regulations.gov
- to ensure that we consider your comment on the draft guidance before we issue the final version, submit comments by July 26, 2017
Thank You
ESI: Listeria

Environmental Surveillance and Investigation: Tools for Listeria Control in the 21st Century
The Race

Prevention

Detection

Concept source: Frank Yiannas
The Facts

- Foodborne outbreak detection is outpacing prevention.
2006 – Mexican-style Restaurant Chain Shredded lettuce, \textit{E. coli} O157:H7
2006 – Tomatoes, \textit{Salmonella} Typhimurium
2006 – Fresh Spinach, \textit{E. coli} O157:H7
2007 – Pizza, \textit{E. coli} O157:H7
2007 – Pot Pies, \textit{Salmonella} I4,[5],12:i-1
2007 – Ground Beef Patties, \textit{E. coli} O157:H7
2007 – Veggie Flavored Rice and Corn Snack, \textit{Salmonella} Wandsworth
2007 – Peanut Butter, \textit{Salmonella} Tennessee
2008 – Raw Produce, \textit{Salmonella} Saintpaul
2008 – Beef, \textit{E. coli} O157:H7
2008 – Rice and Wheat Cereals, \textit{Salmonella} Agona
2008 – Cantaloupe, \textit{Salmonella} Litchfield
2009 – Beef, \textit{E. coli} O157:H7
2009 – Prepackaged Cookie Dough, \textit{E. coli} O157:H7
2009 – Alfalfa Sprouts, \textit{Salmonella} Saintpaul
2009 – Peanut Butter, \textit{Salmonella} Typhimurium
2009 – Pistachios, \textit{Salmonella} (multiple types)
2010 – Alfalfa Sprouts, \textit{Salmonella} I4,[5],12:i-1
2010 – Shell Eggs, \textit{Salmonella} Enteritidis
2010 – Cheese, \textit{E. coli} O157:H7
2010 – Cheesy Chicken Rice Frozen Entrée, \textit{Salmonella} Chester
2010 – Frozen Maney Fruit Pulp, \textit{Salmonella} Typhi
2010 – Mexican-style Restaurant Chain, \textit{Salmonella} Hartford & Baildon
2010 – Alfalfa Sprouts, \textit{Salmonella} Newport
2010 – Shredded Romaine Lettuce, \textit{E. coli} O157:H7
2010 – Red & Black Pepper/Italian-style Meats, \textit{Salmonella} Montevideo
2010 – Beef, \textit{E. coli} O157:H7
2011 – Ground Beef, \textit{Salmonella} Typhimurium
2011 – Kosher Broiled Chicken Livers, \textit{Salmonella} Heidelberg
2011 – Turkish Pine Nuts, \textit{Salmonella} Enteritidis
2011 – Cantaloupe, \textit{Listeria monocytogenes}
2011 – Ground Turkey, \textit{Salmonella} Heidelberg
2011 – Whole, Fresh Imported Papayas, \textit{Salmonella} Agona
2011 – Alfalfa and Spicy Sprouts, \textit{Salmonella} Enteritidis
2011 – Travel to Germany (Fenugreek Sprouts), \textit{STEC} \textit{E. coli} O104
2011 – Turkey Burgers, \textit{Salmonella} Hadar
2011 – Lebanon Bologna, \textit{E. coli} O157:H7
2011 – Cantaloupe, \textit{Salmonella} Panama
2011 – Hazelnuts, \textit{E. coli} O157:H7
2012 – Spinach & Spring Mix, \textit{E. coli} O157:H7
2012 – Peanut Butter, \textit{Salmonella} Bredeney
2012 – Ricotta Salata Cheese, \textit{Listeria monocytogenes}
2012 – Mangoes, \textit{Salmonella} Bredeney
2012 – Cantaloupe, \textit{Salmonella} Typhimurium and Newport
2012 – Ground Beef, \textit{Salmonella} Enteritidis
2012 – Raw Scraped Ground Tuna, \textit{Salmonella} Bareilly and Nchanga
2012 – Raw Clover Sprouts, \textit{E. coli} O26
2012 – Mexican-style Restaurant Chain, \textit{Salmonella} Enteritidis
2013 – Ready-to-Eat Salads, \textit{E. coli} O157:H7
2013 – Chicken, \textit{Salmonella} Heidelberg
2013 – Raw Shellfish, \textit{Vibrio parahaemolyticus}
2013 – Fresh Produce, \textit{Cyclospora}
2013 – Cheese, \textit{Listeriais}
2013 – Pomegranate Seeds, \textit{Hepatitis A}
2013 – Tahini Sesame Paste, \textit{Salmonella} Montevideo and Mbandaka
2013 – Cucumbers, \textit{Salmonella} Saintpaul
2013 – Frozen Food Products, \textit{E. coli} O121
2013 – Chicken, \textit{Salmonella} Heidelberg
2013 – Ground Beef, \textit{Salmonella} Typhimurium
2014 – Cucumbers, \textit{Salmonella} Newport
2014 – Commercially Produced, Prepackaged Caramel Apples, \textit{Listeria monocytogenes}
2014 – Bean Sprouts, \textit{Salmonella} Enteritidis
2014 – Bean Sprouts, \textit{Listeria monocytogenes}
2014 – Cheese, \textit{Listeria monocytogenes}
2014 – Cilantro, \textit{Cyclospora}
2014 – Nut Butter, \textit{Salmonella} Braenderup
2014 – Organic Sprouted Chia Powder, \textit{Salmonella} Newport, Hartford & Oranienburg
2014 – Raw Clover Sprouts, \textit{E. coli} O212
2014 – Ground Beef, \textit{E. coli} O157:H7
2014 – Dairy Products, \textit{Listeria monocytogenes}
2014 – Chicken, \textit{Salmonella} Heidelberg
2014 – Raw Cashew Cheese, \textit{Salmonella} Stanley
2015 – Raw Sprouted Nut Butter Spreads, \textit{Salmonella} Paratyphi B variant L(+)+ tartrate (+)
2015 – Rotisserie Chicken Salad, \textit{E. coli} O157:H7
2015 – Mexican-style Restaurant Chain, \textit{E. coli} O26
2015 – Soft Cheeses, \textit{Listeria monocytogenes}
2015 – Cucumbers, \textit{Salmonella} Poona
2015 – Pork, \textit{Salmonella} I4,[5],12:i-1
2015 – Raw, Frozen, Stuffed Chicken Entrees, \textit{Salmonella} Enteritidis
2015 – Raw, Frozen, Stuffed Chicken Entrees, \textit{Salmonella} Enteritidis
2015 – Frozen Raw Tuna, \textit{Salmonella} Weltevreden and \textit{Salmonella} Paratyphi B variant L(+)+ tartrate (+)
2015 – Ice Cream, \textit{Listeria monocytogenes}
2016 – Shell Eggs, \textit{Salmonella} Oranienburg
2016 – Beef Products, \textit{E. coli} O157:H7
2016 – Frozen Strawberries, \textit{Hepatitis A}
2016 – Frozen Scallops, \textit{Hepatitis A}
2016 – Alfalfa Sprouts, \textit{Salmonella} Reading and Abony
2016 – Flour, \textit{E. coli} O121 and O26
2016 – Frozen Vegetables, \textit{Listeria monocytogenes}
2016 – Raw Milk, \textit{Listeria monocytogenes}
2016 – Pistachios, \textit{Salmonella} Montevideo
2016 – Alfalfa Sprouts, \textit{E. coli} O157
2016 – Alfalfa Sprouts, \textit{Salmonella} Muenchen and Kentucky
2016 – Organic Shake & Meal Products, \textit{Salmonella} Virchow
2016 – Packaged Salads, \textit{Listeria monocytogenes}
2017 – Vulto Creamery Soft Raw Milk Cheese, \textit{Listeria monocytogenes}

\textbf{N = 98}
2006 – Mexican-style Restaurant Chain Shredded lettuce, *E. coli* O157:H7
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2007 – Ground Beef Patties, *E. coli* O157:H7
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2009 – Beef, *E. coli* O157:H7
2009 – Prepackaged Cookie Dough, *E. coli* O157:H7
2009 – Alfalfa Sprouts, *Salmonella Saintpaul*
2009 – Peanut Butter, *Salmonella Typhimurium*
2009 – Pistachios, *Salmonella* (multiple types)
2010 – Alfalfa Sprouts, *Salmonella I4,[5],12:i-*
2010 – Shell Eggs, *Salmonella Enteritidis*
2010 – Cheese, *E. coli* O157:H7
2010 – Cheesy Chicken Rice Frozen Entrée, *Salmonella Chester*
2010 – Frozen Marney Fruit Pulp, *Salmonella Typhi*
2010 – Mexican-style Restaurant Chain, *Salmonella* Hartford & Baildon
2010 – Alfalfa Sprouts, *Salmonella Newport*
2010 – Shredded Romaine Lettuce, *E. coli* O157:H7
2010 – Beef, *E. coli* O157:H7
2011 – Ground Beef, *Salmonella Typhimurium*
2011 – Romaine Lettuce, *E. coli* O157:H7
2011 – Kosher Broiled Chicken Livers, *Salmonella* Heidelberg
2011 – Turkish Pine Nuts, *Salmonella Enteritidis*
2011 – Cantaloupe, *Listeria monocytogenes*
2011 – Ground Turkey, *Salmonella* Heidelberg
2011 – Whole, Fresh Imported Papayas, *Salmonella Agona*
2011 – Alfalfa and Spicy Sprouts, *Salmonella Enteritidis*
2011 – Travel to Germany (Fenugreek Sprouts), STEC *E. coli* O154
2011 – Turkey Burgers, *Salmonella* Hadar
2011 – Lebanon Bologna, *E. coli* O157:H7
2011 – Cantaloupe, *Salmonella Panama*
2011 – Hazelnuts, *E. coli* O157:H7
2011 – Spinach & Spring Mix, *E. coli* O157:H7
2012 – Peanut Butter, *Salmonella* Breedeney
2012 – Ricotta Salata Cheese, *Listeria monocytogenes*
2012 – Mangos, *Salmonella* Breedeney
2012 – Cantaloupe, *Salmonella Typhimurium* and *Newport*
2012 – Ground Beef, *Salmonella Enteritidis*
2012 – Raw Clover Sprouts, *E. coli* O212
2012 – Mexican-style Restaurant Chain, *Salmonella Montevideo*
2013 – Prepackaged Lettuce, *E. coli* O157:H7
2013 – Fresh Produce, *Salmonella Enteritidis*
2013 – Cheese, *Listeria*
2013 – Fresh Produce, *Cyclospora*
2013 – Pomegranate Seeds, *Hepatitis A*
2013 – Cucumbers, *Salmonella Saintpaul*
2013 – Frozen Food Products, *E. coli* O121
2013 – Chicken, *Salmonella* Heidelberg
2013 – Ground Beef, *Salmonella Typhimurium*
2014 – Cucumbers, *Salmonella Newport*
2014 – Commercially Produced, Prepackaged Caramel Apples, *Listeria monocytogenes*
2014 – Bean Sprouts, *Salmonella Enteritidis*
2014 – Bean Sprouts, *Listeria monocytogenes*
2014 – Cheese, *Listeria monocytogenes*
2014 – Chicarito, *Cyclospora*
2014 – Nut Butter, *Salmonella* Braenderup
2014 – Organic Sprouted Chia Powder, *Salmonella Newport, Hartford & Oranienburg*
2014 – Raw Clover Sprouts, *E. coli* O212
2014 – Ground Beef, *E. coli* O157:H7
2014 – Dairy Products, *Listeria monocytogenes*
2014 – Chicken, *Salmonella Heidelberg*
2014 – Raw Cashew Cheese, *Salmonella* Stanley
2015 – Raw Sprouted Nut Butter Spreads, *Salmonella Paratyphi B* variant L(+) tartrate (+)
2015 – Rotisserie Chicken Salad, *E. coli* O157:H7
2015 – Mexican-style Restaurant Chain, *E. coli* O26
2015 – Soft Cheeses, *Listeria monocytogenes*
2015 – Cucumbers, *Salmonella Poona*
2015 – Pork, *Salmonella I4,[5],12:i-*
2015 – Raw, Frozen, Stuffed Chicken Entrees, *Salmonella Enteritidis*
2015 – Raw, Frozen, Stuffed Chicken Entrees, *Salmonella Enteritidis*
2015 – Frozen Raw Tuna, *Salmonella* Weltevreden and *Salmonella Paratyphi B* variant L(+) tartrate (+)
2015 – Ice Cream, *Listeria monocytogenes*
2016 – Shell Eggs, *Salmonella* Oranienburg
2016 – Beef Products, *E. coli* O157:H7
2016 – Frozen Strawberries, *Hepatitis A*
2016 – Frozen Scallops, *Hepatitis A*
2016 – Alfalfa Sprouts, *Salmonella* Reading and Abony
2016 – Flour, *E. coli* O121 and O26
2016 – Frozen Vegetables, *Listeria monocytogenes*
2016 – Raw Milk, *Listeria monocytogenes*
2016 – Pistachios, *Salmonella Montevideo*
2016 – Alfalfa Sprouts, *E. coli* O157
2016 – Alfalfa Sprouts, *Salmonella Muenchen and Kentucky*
2016 – Organic Shake & Meal Products, *Salmonella* Virchow
2016 – Packaged Salads, *Listeria monocytogenes*
2017 – Vulto Creamery Soft Raw Milk Cheese, *Listeria monocytogenes*

N= 98
Foodborne outbreak detection is outpacing prevention.

Whole genome sequencing and next-generation sequencing technologies are expected to continue to increase the number of outbreaks which will be detected.
Outbreaks by Year
Average Cases per Outbreak

2006 → 151

2016 → 21
The Facts

- Foodborne outbreak detection is outpacing prevention.
- Whole genome sequencing and next-generation sequencing technologies are expected to continue to increase the number of outbreaks which will be detected.
- Need more practical application from research
- The industry needs to evolve
Insanity: doing the same thing over and over again and expecting different results.

- Albert Einstein
Surveillance and Investigation Tools

- Speciation
- Visual Mapping
- PFGE
- WGS
- Microbiome analysis
- Metagenomics
Visual Mapping
Listeria monocytogenes Suspects confirmed negative Salmonella Non-pathogenic Listeria species

Note: map has been created for demonstration only and does not reflect any actual or real data
Pulsed Field Gel Electrophoresis

- PFGE separates large DNA Molecules to provide a DNA fingerprint
Whole Genome Sequencing

- WGS provides a very precise DNA fingerprint by determining the order of the bases within the genome of an organism.
Microbiomes are communities of organisms present in an environment.
Microbiome “profiling”
Thank You

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Listeria Workshop at Food Safety Summit

Ozgur Koc

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About Crunch Pak

• What do we do? Fresh Cut Apple Slicing

• To give a visual of what Crunch Pak produces each year; if you laid the slices end to end, they would wrap around the world, 2 ½ times, or 63,604 miles.

• OR, if you take since we started, you could go to the moon and back twice…that’s a lot of apple slices…

• 100% vertically integrated with organics

• Food Safety Program build based on a USDA CRADA Study
• Food Safety at Crunch Pak (before recall)
  • 3rd Party GFSI Audits
  • All raw product is sourced from packing houses with third party GAP audits & SQF Level 2 Certified
  • At least 25 audits a year by customer and third parties
  • Pass all requisite audits with excellent scores
Case Study

11/13/2013

• Phone call from WSDA; XSDA sampled 1 bag of 14oz tart, tested positive for Listeria

• Steps under our control/Actions Taken

  • Traceback started for affected product

  • Identify if we have any raw apples in our inventory from the same lot

  • Our listeria sampling results from non-food surface contact areas show negative results for day of manufacture, October 24th day before and day after.

  • Complete excessive sanitation and complete excessive Listeria sampling program before production and during production to identify any weak spot in the system
Chronology of Events, cont.

11/14/2013
• Crunch Pak starts extensive listeria sampling totaling 135 swabs per day (before recall -30)
• FDA/WSDA teams arrive for onsite inspection and investigation

11/15/2013
• FDA conducted sampling of 34 food surface and non-food contact locations – all negative

11/16/2013
• WSDA results negative from products sampled from retail
  • 10 bags with 8 different expiration dates
• CP duplicate samples of retains and WSDA samples are negative
  • 15 bags same production day including 2 retains from the same bagger MDA found positive
  • Packed 4 minutes before and 58 minutes later from the same bagger /found positive
Chronology of Events, cont.

11/18/2013

- FDA conducted sampling of 80 food surface and non-food contact locations – all negative

11/19/2013

- A customer of CP under Private Label sends their team visits for audit and composite sampling of food and non-food surface locations – all negative

11/21/2013

- FDA/WSDA concluded investigation and finalized reports
- No official action indicated with their report. There will not be an FDA warning letter sent to us.
Chronology of Events, cont.

• What does all test (WSDA & CP Finished Product, FDA, Private Label environmental swabs from food and non food surface contact areas) results mean?
  • Listeria is sporadic
• Listeria is in our environment
• We need to find and control it
Conclusions to Date (11/23/2013)

Revisit Test Results

- WSDA -10 Finished Products tested
  - 8 different pack dates with product coming from different lines
- Crunch Pak 15 Retains matching WSDA samples
  - including 2 bags from the bagger
    - 4 minutes before
    - 58 minutes after
- FDA Test Results
  - Food and non food surface contact areas
  - 114 Samples
  - Before and during production
- Private Label Consultant
  - 16 samples
Conclusions to Date, cont.

• 13 recalls in the USA related to sliced apples since 2009
  • At least 1 recall per year related with Sliced Apples
  • All L.Mono
For Cause Investigation

• Seek & Destroy Team

• What could have caused recall? Is the system effective to control system
  • Raw Product
  • Equipment Design
  • Sanitation
  • Facility Maintenance
  • Employee Practices
  • False Positive
    • Sampling and Testing Protocol
Focus on Prevention and Control

• Supply Chain
• Sanitary Design
• Sanitation
• Employee and Manufacturing Practices Verification through testing:
Recommendations for other Fresh Cut suppliers

• Raw Apple Supplier Review
  • Apple Supplier Environmental Monitoring Program
  • Sanitation Program & Sanitary Design
  • Apple Supplier Flume System Review and Validation Studies
  • Bin preventative maintenance
  • Post Harvest Practices
  • Use your resources to educate them
Cores are divided up into 2 bags. Bags are labeled with Crunch Pak lot number.
Recommendations for other Fresh Cut suppliers

- It is worthwhile to consult with Listeria control “experts”
- Experience in meat/seafood industries
- Experts in sanitary design
- Someone who has fought the war on Listeria
- Do not disregard expert recommendations just because they don’t fit your business model
Recommendations for other Fresh Cut suppliers

• Ensure your environmental monitoring program is robust
• Design a program based on your process and environment
• Understand “hot spots” in your facility as well as those in other RTE industries
  • Previously drains
  • What is around it?
• Aggressive follow up to any positive
Recommendations for other Fresh Cut suppliers

• Sanitation is a complex process and should not be taken lightly.
• The entire management team should understand the chemicals and processes that are used and why
• Regular management assessment of sanitation practices are critical
• Make management aware of sanitation metrics
• Remain knowledgeable of next generation sanitation innovations
• Do not allow Listeria to get a foot hold.
Recommendations for other Fresh Cut suppliers

- Understand sanitary design of equipment and facility
  - Review Niche & Harborage Areas (Top and bottom of Slicers, Inside of Shaker)
- Complete a full assessment of your equipment and facility as part of your HACCP plan
- Remove harborage points and make repairs as needed
- Employ or consult with a sanitary design expert.
Recommendations for other Fresh Cut suppliers

• Understand sanitary design of equipment and facility
• Complete a full assessment of your equipment and facility as part of your HACCP plan
• Remove harborage points and make repairs as needed
• Employ or consult with a sanitary design expert.
Recommendations for other Fresh Cut suppliers

- Food Safety Culture Survey
- Do not underestimate the impact of each employee to control Listeria in the facility
- Regular, repeated training on the importance of Listeria control
- Understand people, equipment, and utensil traffic flow in every part of the facility.
Items Being Implemented and Addressed to Prevent Reoccurrence

• Process Control Initiatives
  • Raw Product Process Control Testing: Testing Indicators
  • Environmental Monitoring Program: Daily Listeria Swabs from Non Food Surface Contact Area
  • Weekly Slicing Machine Oil/Grease Micro Sampling for APC and Listeria
  • Finished Product Testing
Recent Listeriosis Outbreak Investigations and the Growing Impact of Whole Genome Sequencing

Matthew Wise, MPH, PhD
Outbreak Response Team Lead
Outbreak Response and Prevention Branch
Division of Foodborne, Waterborne, and Environmental Diseases

Pre-Conference Workshop: The Latest in Listeria Control
Food Safety Summit, Chicago, IL
May 2017
Listeriosis in the United States: Epidemiology and Clinical Manifestations

- 1,600 invasive infections estimated to occur annually:
  - Nearly all hospitalized
  - Resulting in over 250 deaths

- Groups at higher risk for infection or serious illness:
  - Pregnant women and newborns
  - Older adults
  - Immunocompromised persons

- Infection can cause:
  - Miscarriages and stillbirths in pregnant women
  - Serious illness or death in newborns
  - Sepsis or meningitis in older adults
The *Listeria* Initiative

- Because of the severity of listeriosis, state and local health departments prospectively interview all patients
  - Using a standard form
  - Whether or not part of an outbreak

- Assists outbreak investigations in two major ways
  - Early hypothesis generation
  - Provides “controls” for case-case analytic methods
Detecting Outbreaks with PulseNet

- Subtyping enteric bacteria is essential to identifying highly disseminated outbreaks
- PulseNet laboratory network established in 1996
  - Over 80 participating laboratories in the US
  - 60,000+ isolates subtyped annually
- Bacteria collected from ill people undergo DNA “fingerprinting” using pulse-field gel electrophoresis (PFGE)

Bacteria with the same “fingerprint” are more likely to come from a common source
Conceptual Framework for PFGE Subtyping

Comparing isolates is analogous to comparing two books based on the number of words in each chapter.

Other lab workflows needed for serotype, virulence factors, etc.
PFGE and *Listeria monocytogenes*

- 573 non-outbreak isolates in PulseNet in 2015:
  - 375 PFGE pattern combinations (2 enzyme)
  - 21 pattern combinations account for 25% of isolates
WGS Provides a Higher Resolution View of the Bacterial Genome

PFGE only gives information at a “cut” site via the banding pattern

WGS has the ability to give us information at nearly every position in the bacterial genome

Comparing isolates is analogous to comparing two books based on all the words in the book

Serotype, virulence, etc. can be identified in one workflow
Whole Genome Sequencing (WGS) *Listeria* Pilot Project

- Started September 2013
- Goal: Sequence all *Listeria monocytogenes* clinical, food, and environmental isolates
- Near real-time (<1 week for patient isolates)
Why focus on *Listeria* first for WGS?

- Illness is rare but serious, costly, and commonly outbreak associated
- Current subtyping methods are not ideal
- *Listeria* genome is fairly small and relatively easy to sequence and analyze
- Strong epidemiologic surveillance (*Listeria* Initiative)
- Strong regulatory component
RECENT LISTERIOSIS OUTBREAKS
## Recent Multistate Listeriosis Outbreak Investigations

<table>
<thead>
<tr>
<th>Year</th>
<th>Vehicle</th>
<th>States</th>
<th>Cases</th>
<th>Deaths</th>
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<tr>
<td>2017</td>
<td>Gourmet Soft Raw Milk Cheese</td>
<td>4</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>2016</td>
<td>Frozen Vegetables</td>
<td>4</td>
<td>9</td>
<td>3</td>
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<tr>
<td>2016</td>
<td>Raw Milk</td>
<td>2</td>
<td>2</td>
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<tr>
<td>2016</td>
<td>Bagged Salad Mixes</td>
<td>9</td>
<td>19</td>
<td>1</td>
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<tr>
<td>2015</td>
<td>Middle Eastern-Style Soft Cheese</td>
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<td>30</td>
<td>3</td>
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<tr>
<td>2015</td>
<td>Ice Cream</td>
<td>4</td>
<td>10</td>
<td>3</td>
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<tr>
<td>2014</td>
<td>Caramel Apples</td>
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<td>35</td>
<td>7</td>
</tr>
<tr>
<td>2014</td>
<td>Mung Bean Sprouts</td>
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</tr>
<tr>
<td>2014</td>
<td>Hispanic-Style Cheese</td>
<td>4</td>
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<td>1</td>
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<tr>
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<td>Hispanic-Style Cheese</td>
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<td>2013</td>
<td>Gourmet Soft Cheese</td>
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<td>2012</td>
<td>Imported Ricotta Salata Cheese</td>
<td>14</td>
<td>22</td>
<td>4</td>
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<tr>
<td>2011</td>
<td>Cantaloupes (Domestic)</td>
<td>28</td>
<td>147</td>
<td>33</td>
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</tbody>
</table>
Listeriosis and Caramel Apples
Outbreak Identification: Listeriosis and Caramel Apples

- Two listeriosis illness clusters identified in November 2014
  - Cluster 1: Arizona and New Mexico contact CDC regarding an increase in listeriosis cases in both states
  - Cluster 2: PulseNet identifies a second cluster of 4 listeriosis cases in Minnesota and Missouri

- Isolates within each cluster were closely related to one another by wgMLST, but the two clusters were not closely related genetically
Outbreak Identification: Listeriosis and Caramel Apples

- Clusters combined into one investigation
  - Similar timing and geographic distribution
  - One patient had isolates with both PFGE patterns
Hypothesis Generation: Listeriosis and Caramel Apples

- No strong epidemiologic signal from initial interview of ill people
  - All cases were interviewed with the standard *Listeria* Initiative questionnaire
  - Moved to interviews with the broader National Hypothesis Generating Questionnaire, which also did not yield a strong hypothesis

- CDC then asked the states if we could perform single-interviewer open-ended interviews
  - On December 15, during a interview with a patient’s spouse, a local TX official asked: “Did your spouse eat any seasonal items like caramel apples?”
Hypothesis Testing: Listeriosis and Caramel Apples

- Compared apple and caramel apple consumption among outbreak cases to ill people with unrelated listeriosis

<table>
<thead>
<tr>
<th></th>
<th>Outbreak Cases</th>
<th>Non-outbreak Cases*</th>
<th>p-value</th>
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</thead>
<tbody>
<tr>
<td>Caramel Apples</td>
<td>28/31 (90%)</td>
<td>1/36 (3%)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Whole Apples</td>
<td>9/16 (56%)</td>
<td>20/30 (67%)</td>
<td>0.1370</td>
</tr>
</tbody>
</table>

*Ill persons with unrelated *Listeria* infections during the same time period
Communication: Listeriosis and Caramel Apples

- To prevent additional illnesses, CDC felt it was important to communicate even though a specific brand of caramel apples had not yet been identified.

- CDC tries to be as specific as possible about food items; rarely publicly implicates generic food products.

- Although “caramel apples” is a generic food product, CDC was able to specify:
  - Commercially produced
  - Prepackaged
  - Not homemade
Traceback: Listeriosis and Caramel Apples

- FDA and partners collect samples:
  - Apple supplier
  - Caramel apple production facilities
  - Whole apples in the distribution chain
WGS Results: Listeriosis and Caramel Apples

- 50 isolates sequenced
  - Clinical isolates from ill people
  - Grower A food contact surfaces
  - Grower A packing line floor drain
  - Grower A apples collected in the distribution chain

- Fell into 2 WGS clades, each containing closely related clinical and food/environmental isolates
Why Caramel Apples?

- The acidity of apples and low water activity of caramel should not support growth of *L. monocytogenes*

- However, *L. monocytogenes* inoculation studies showed a >3 log$_{10}$ increase in 3 days on unrefrigerated caramel apples with sticks
  - Less growth at refrigerator temperatures; no growth on caramel apples without sticks
  - Hypothesis: insertion of the stick into the apple allows juice to enter the space between the caramel and the skin of the apple

Listeriosis and Ice Cream
February 2015: Ice Cream Testing

- *Listeria monocytogenes* identified in multiple samples of 2 different products collected for routine sampling by South Carolina:
  - 7 distinct *Listeria* pulsed-field gel electrophoresis (PFGE) patterns
  - Both made on one line at a Texas Blue Bell facility

- Texas collects products for testing from the facility
  - Identified *Lm* in the same two products as in South Carolina
  - Also found in ice cream “Scoops” produced on same line
  - Same PFGE patterns as found in South Carolina
March 2015: Kansas Investigation

- Two patients infected with *Listeria* with indistinguishable PFGE patterns in late 2014 and early 2015
  - Both in same hospital *before* listeriosis onset for unrelated problems

- 3 other patients were in the same hospital before listeriosis onset in the previous year
  - Each infected with different PFGE patterns

- Entire state has median of only 4 listeriosis cases/year
Whole Genome Sequencing and Epidemic Curve
Kansas, 2014–2015

- 4/4 patients with available hospital dietary records consumed milkshakes made with Blue Bell “Scoops”
- 4/5 isolates match PFGE patterns found in ice cream

Number of Illnesses

Month of Illness Onset

<table>
<thead>
<tr>
<th>Jan-14</th>
<th>Feb-14</th>
<th>Mar-14</th>
<th>Apr-14</th>
<th>May-14</th>
<th>Jun-14</th>
<th>Jul-14</th>
<th>Aug-14</th>
<th>Sep-14</th>
<th>Oct-14</th>
<th>Nov-14</th>
<th>Dec-14</th>
<th>Jan-15</th>
<th>Feb-15</th>
</tr>
</thead>
</table>

- 4/4 patients with available hospital dietary records consumed milkshakes made with Blue Bell “Scoops”
- 4/5 isolates match PFGE patterns found in ice cream
Multiple PFGE patterns seen among ice cream isolates, but all isolates closely related by WGS (maximum 28 allele difference)

Patient isolates closely related to ice cream isolates from the Texas production facility

Four Kansas patient isolates that were closely related by WGS
Testing at the Kansas Hospital

- Kansas Department of Health and Environment collects Blue Bell ice cream from affected hospital
  - March 22: *Listeria* found in 3 oz. chocolate ice cream cup made in Blue Bell’s Oklahoma facility

- March 23: Blue Bell recalls ice cream cups from their Oklahoma facility

**FDA: Recall expanded for Blue Bell Ice Cream products**
Illnesses Linked to Blue Bell Oklahoma Facility?

- PFGE pattern determined for *Listeria* from chocolate cup
- Pattern only seen 6 times before, all from patients, 2010–2014
- All patients previously hospitalized
- Exposure to ice cream uncertain, though all hospitals received Blue Bell ice cream
April 2015: Listeriosis Cases Linked to Ice Cream from the Oklahoma Facility Using WGS
wgMLST Tree with All Patient and Ice Cream Isolates

Isolates from KS patients and TX facility products all closely related (2014-2015)

Isolates from AZ, TX, and OK patients closely related to isolates from OK facility products (2010-2015)
Listeriosis and Frozen Vegetables
Outbreak Identification

- In March 2016, CDC PulseNet identified a cluster of 8 *Listeria monocytogenes* infections
  - Clinical isolates highly related to one another by WGS
  - Cluster identified earlier in 2016, but no investigation opened
- Also closely related by WGS to two environmental isolates
  - Collected by FDA from a frozen fruit and vegetable processing facility in Oregon in March 2016
Initial Product Actions

- The frozen fruit and vegetable processor conducts a voluntary market withdrawal on the basis of:
  - FDA inspectional findings
  - *Lm* isolated from the production environment, and
  - The identification of closely related clinical isolates

- On April 10 the first indication of product actions becomes public via a downstream recall by Schnucks
Interview Data: Finding an Food Signal

- CDC develops a supplemental questionnaire
  - Environmental isolates allow for more targeted questions about frozen fruits and vegetables

- Four ill people interviewed were able to provide shopper card data
  - Important because illnesses had occurred months to years in the past
  - 3/4 ate frozen vegetables in the month prior to becoming ill
  - One ill person still had leftovers in the freezer
Product Testing

- Outbreak strains of *Listeria* identified in open and unopened bags of two brands of frozen vegetables
  - One frozen vegetable mix brand from an ill person’s home in California
  - Routine retail samples of another brand of frozen peas and frozen corn in Ohio

- Both brands produced by the same firm
  - Received frozen vegetables from the Oregon processing facility where *Listeria* was identified in the environment
<table>
<thead>
<tr>
<th>No.</th>
<th>PFGE-Apal-pattern</th>
<th>Outbreak</th>
<th>SampleType</th>
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<th>SourceCountry</th>
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<th>Modified Date</th>
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<th>IsolateDate</th>
<th>SourceCountry</th>
<th>SourceSite</th>
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<th>Modified Date</th>
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<td>0101</td>
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<td>2/1a</td>
<td>Environmental Swab</td>
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<td>Routine product sampling in OH</td>
<td>FCF__949810 - 104 - 164</td>
<td>2016-03-08</td>
</tr>
</tbody>
</table>

**Legend:**
- **Initial 8 patient isolates from frozen vegetable products (no clinical isolates):** 
  - Frozen vegetable products
  - Leftover from CA patient
- **Additional environmental isolates from the frozen fruit and vegetable processor:**
  - Frozen vegetable products
  - Leftover from CA patient
- **Initial 8 environmental isolates:**
  - Frozen vegetable products
  - From the frozen fruit and vegetable processor
- **Routine product sampling in OH:**
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
- **Outbreak:**
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
- **SourceSite:**
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
- **SourceCountry:**
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
  - Frozen vegetable products
Resolution of the Outbreak

- Relatively small number of illnesses led to recalls of 456 products sold under 42 brands
  - Recalled products not limited to frozen vegetables and fruits, and included foods like prepared salads, frozen meals, frozen snack foods
- However, if this had not been identified, low numbers of illnesses could likely have continued indefinitely
- Were not able to obtain good information on how these food were prepared
  - Microwaving vs cooking?
  - Eaten raw or used in smoothies?
Emerging Trends in Listeriosis Outbreaks

- Many novel vehicles identified since implementation of WGS in 2013
  - Caramel apples
  - Ice cream
  - Frozen vegetables
  - Bagged salad mix

- Outbreaks continue to be linked to cheese, primarily from domestically produced pasteurized milk cheeses

- Notable absence of hot dogs/deli meats as a source of major outbreaks over the last decade
Changing Notion of Sporadic Illness

Listeriosis linked to frozen vegetables
• 9 cases in 3 years

These illnesses are not sporadic, but are endemic disease that previously appeared sporadic because of limitations in investigation tools

Listeriosis linked to ice cream
• 10 cases in 5 years
Public Health Impact of WGS on Listeriosis Outbreak Investigations

<table>
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<tr>
<th></th>
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<tbody>
<tr>
<td>No. of clusters detected</td>
<td>14</td>
<td>19</td>
<td>21</td>
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<tr>
<td>No. of clusters detected sooner or only by WGS</td>
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<td>6</td>
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<tr>
<td>No. of outbreaks solved (food source identified)</td>
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<tr>
<td>Median no. of cases per cluster or outbreak</td>
<td>6</td>
<td>4</td>
<td>3</td>
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<tr>
<td>No. of cases linked to food source</td>
<td>13</td>
<td>20</td>
<td>103</td>
</tr>
</tbody>
</table>
Summary

- WGS has already improved our ability to detect, triage, investigate, and solve outbreaks of *Listeria monocytogenes* infections
  - More outbreaks found
  - Identified when they are smaller
  - Begin the investigation with better “leads”
  - Hopefully stopped sooner, before they become catastrophic (e.g., 2011 cantaloupe outbreak)

- The vast majority of listeriosis in the US is still not linked to a known outbreak
  - The next steps in preventing illness will need to target what have, until now, appeared to be sporadic illnesses