Quantitative Assessment of the Risk of Listeriosis from Soft-ripened Cheese Consumption in the United States and Canada.

Régis Pouillot\textsuperscript{1}, Loan Nguyen\textsuperscript{2}, Sherri Dennis\textsuperscript{1}

\textsuperscript{1} FDA/CFSAN, USA
\textsuperscript{2} Health Canada - Santé Canada
Background

• The United States and Canada continue to experience sporadic illness and outbreaks of listeriosis associated with the consumption of cheese
• FDA and Health Canada (HC) continue to evaluate the safety of cheese, particularly cheese made from unpasteurized milk

FDA and HC carried out a QMRA to evaluate the effectiveness of and the public health impact of processing and intervention strategies to reduce or prevent *Listeria monocytogenes* in soft-ripened cheeses.
Scope

• **Pathogen:** *Listeria monocytogenes*
• **Food:** Camembert, as an example of soft-ripened cheese
• **Population of Interest:**
  – General population of the U.S. and Canada
  – Subpopulations identified as at-risk in both countries
• **Endpoint:** Invasive listeriosis
• (primary) **Risk metric:** Probability of invasive listeriosis per soft-ripened cheese serving
• **Baseline**
  – “Pasteurized-milk cheese”, *i.e.* Soft-ripened cheese made from pasteurized milk, “stabilized process”

  Vs.

• **Alternatives**
  – “Raw-milk cheese”, *i.e.* Soft-ripened cheese made from raw milk, “traditional process”, Farmstead scale

  – “Raw-milk cheese” or “Pasteurized-milk cheese” according to various mitigation strategies
Framework / Model / Data

- Framework: *Codex Alimentarius*, FDA, HC

  - Exposure assessment
    - *L. monocytogenes* consumed
  - Hazard Characterization
    - Dose Response

- Fully quantitative risk assessment
  - Second-order Monte Carlo simulation

- Model structure based on
  - Literature, Previous risk assessments, Expert sources

- Data based on
  - Literature, Government surveys, Specific expert elicitations
Hazard Characterization

- Dose Response -

- Adapted from the FAO/WHO (2004) risk model
- Exponential dose-response models considering uncertainty

![Graph showing dose-response relationship with log10(prob of illness) and log10(Dose).]

Blue: Susceptible population
Red: Non-susceptible population
Exposure assessment
*L. monocytogenes* consumed

- **On Farm**
  - (Cross) contamination
  - Growth
  - Mixing
  - Removal

- **Cheese Processing**
  - Growth
  - Inactivation
  - Mixing
  - Partitioning
  - Removal
  - Cross Contamination

- **Transport and Marketing**
  - Growth

- **At Retail**
  - Growth

- **At Home**
  - Growth
  - Partitioning
Baseline Model

- No bacteria from milk ("full" pasteurization)
- Environmental contamination before aging
  - Prevalence and level inferred from Gombas et al, 2003 (+ backcalculation)
- Bacterial growth from contamination to consumption
  - Lag phase: Relative Lag Time concept
  - Growth during ripening: complex model considering T, pH, a_w and interactions
  - Growth during aging: square root model
  - Growth in solid media (vs. liquid) is considered
  - Parameters: meta-analysis of the available literature data
- Partition from serving to serving
Environmental Contamination

Inferences

Prevalence of contaminated cheeses in North-America

Prevalence of contaminated cheeses in North-America at retail
Beta(\(\alpha, \beta\))

Gombas et al. (2003)

\(Lm\) concentration in North-America at retail
\(\ln(c) \sim \text{Normal}(\mu, \sigma^2)\)

Number of \(Lm\) in a 250g cheese at retail in North-America

Number of \(Lm\) in a 250g cheese before aging

Growth during aging

Growth during marketing

Growth during storage at retail

Retail

Manufacturing

Number of \(Lm\) in a 250g cheese before aging

Prevalence of contaminated cheeses before aging

Simulations

Prevalence of contaminated cheeses at retail
Alternative Scenario: Raw-milk Cheeses

- Includes a farm model with
  - Mastitic cows and/or environmental contamination on farm
  - Mixing of milk from various cows
  - Growth in milk: in farm tank, tanker truck and dairy silo
- Growth in cheese considers the lower pH in “traditional” cheese process and regulatory requirement of at least 60 days storage prior to retail
- Considering additionally
  - Partition during cheese formation
  - Inactivation / Growth in cheeses during ripening
Milk Contamination

Process

Quarter 1
Quarter 2
Quarter 3
Quarter 4
Cow 1
Cow 2
Cow ...
Farm 1
Farm 2
Tanker truck
Dairy silo

Data

- Level of contamination in raw milk from mastitic cow
- Number of infected quarters given mastitis
- Yield reduction given mastitis
- Probability of mastitis in the herd given a positive bulk tank
- Number of mastitic cows on *L. monocytogenes* positive farm
- Number of cows per farm
- Milk production
- Prevalence of positive farm bulk tank
- Level of contamination in positive bulk tank
- Storage time and temperature in farm bulk tank
- Growth characteristics
- Storage time and temperature in tanker truck
- Storage time and temperature in dairy silo
Other Alternative Scenarios

- Raw-milk cheese, no 60-day aging restriction
- Raw-milk cheese, mild treatment that reduces the bacterial load in milk by $3 \cdot \log_{10}$
- Raw-milk cheese, test (and discard if positive) milk at every milking
  - 25 ml of raw milk from the farm tank
- Raw-milk cheese, test (and discard if positive) every lot of cheese
  - Composite sample of 25g from 5 cheeses
RESULTS
Baseline

*L. monocytogenes* cells per gram at process pathway steps in contaminated cheeses

Most of the growth occurs after retail

Mean >> 95th percentile

Great (serving to serving at random) variability in this model
Variability Vs. uncertainty

Variability Ratio \((B/A) = 8\,005\)       Uncertainty Ratio \((C/A) = 9\)
Overall Uncertainty Ratio \((D/A) = 107\,933\)

- Variability $>>$ (considered) Uncertainty in this model
Baseline Results

(fully) pasteurized milk, “stabilized” cheese

<table>
<thead>
<tr>
<th>Estimated number of servings resulting in one case of invasive listeriosis.</th>
<th>Canada</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elderly</td>
<td>138 million</td>
<td>136 million</td>
</tr>
<tr>
<td>Pregnant</td>
<td>56 million</td>
<td>55 million</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>163 million</td>
<td>193 million</td>
</tr>
<tr>
<td>General population</td>
<td>7,290 million</td>
<td>8,644 million</td>
</tr>
</tbody>
</table>
Baseline Results
raw milk, “traditional” cheese

Estimated number of servings resulting in one case of invasive listeriosis.
(X-fold increased risk of invasive listeriosis vs. pasteurized milk soft-ripened cheese).

<table>
<thead>
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<th></th>
<th>Canada</th>
<th>United States</th>
</tr>
</thead>
<tbody>
<tr>
<td>Elderly</td>
<td>2.6 Million servings (×53)</td>
<td>1.2 Million servings (×112)</td>
</tr>
<tr>
<td>Pregnant</td>
<td>1.1 Million servings (×52)</td>
<td>570 000 servings (×96)</td>
</tr>
<tr>
<td>Immunocompromised</td>
<td>2.4 Million servings (×69)</td>
<td>1.2 Million servings (×157)</td>
</tr>
<tr>
<td>General population</td>
<td>105 Million servings (×69)</td>
<td>55 Million servings (×157)</td>
</tr>
</tbody>
</table>
Alternative Scenarios for Raw Milk cheese (Elderly population, Canada)

Mean Risk Higher than Pasteurized-milk

Mean Risk Lower than Pasteurized-milk

- Mean risk per serving
- Mean Reference (Pasteurized milk)
## Alternative Scenarios for Raw Milk cheese (Elderly population, Canada)

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Intra lot contamination</th>
<th>Logistic (Risk per serving)</th>
<th>Mean Risk Higher than Pasteurized-milk</th>
<th>Mean Risk Lower than Pasteurized-milk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pasteurized milk, Baseline</td>
<td></td>
<td></td>
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<tr>
<td>Raw milk, Baseline</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Raw milk, Cheese lot tested (100%)</td>
<td>0.5% (vs. 2.5%)</td>
<td>-8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intra lot contamination</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intra lot contamination</td>
<td>1.0% (vs. 2.5%)</td>
<td>-9</td>
<td></td>
<td></td>
</tr>
<tr>
<td>95% of the lot tested (vs 100%)</td>
<td></td>
<td>-10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>90% of the lot tested (vs 100%)</td>
<td></td>
<td>-10</td>
<td></td>
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</tbody>
</table>

**Legend:**
- Mean risk per serving
- Mean Reference (Pasteurized milk)
SUMMARY - CONCLUSIONS
“Complex Models to Answer Complex Questions”

• Extend the FDA/FSIS 2003 Risk Assessment from “store-to-fork” to “farm-to-fork”

• Comparing risk of listeriosis from pasteurized- vs. raw-milk cheese needed to consider
  – A full farm to fork model
    • Contamination in farm vs. in-plant contamination
  – A complex growth model considering
    • Lag time
    • Traditional vs. Stabilized manufacturing process
    • Interactions between environmental parameters
    • Growth in solid media

• Limitations – Caveats
  – Conclusions limited to the considered pathogen and the considered cheese
  – Dose-response
Take-home message

• Variability in the Risk linked to the subpopulation
  – Within a country: linked to the dose-response
  – Between countries: different consumption pattern, raw-milk prevalence

• Pasteurized-milk cheese:
  – Time / Temperature in refrigerator is the key factor that increases the risk of listeriosis from contaminated cheeses
  – The best strategy is nevertheless to reduce environmental contamination

• The risk from consumption of raw milk made cheeses is much higher than the risk for pasteurized milk cheeses in the U.S. and Canada
  – × 50 to 160 times higher

• The 60 day aging regulation could increase the risk of listeriosis for raw-milk soft-ripened cheeses

• For raw milk made cheeses, testing every cheese lot is the only alternative that reduces the risk below the level of risk observed in pasteurized milk made cheeses
Current / Next step

- Peer reviewed
- Draft report made available
- Public comments
  - Ended April 29th
  - 96 comments posted

- Now Considering the comments
Acknowledgments

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• FDA and HC Risk managers

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