Comparison of the U.S. and FAO/WHO *Listeria monocytogenes* Risk Assessments

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Listeria monocytogenes

- Foodborne bacterium that causes a relatively rare, life threatening disease

- Primarily affects neonates, elderly, individuals with depressed immunity

- Associated with ready-to-eat foods, particularly those refrigerated for extended periods
Risk Assessments

Two risk assessments in final stages
- U.S. DHHS (FDA) and USDA (FSIS)
- FAO/WHO (JEMRA)

Both are risk ranking risk assessments focused on ready-to-eat foods
Developed to answer different risk management questions
FDA/FSIS Risk Assessment
The *Listeria* “Problem”

Improve public health by determining which foods should receive the most regulatory attention
Selection of Food Categories

- Potential for *L. monocytogenes* contamination
- Ready-to-eat (with one exception, foods not cooked just prior to consumption)
- History of causing listeriosis
- Food contamination and consumption data
- Individual foods grouped into categories (23)
Populations Studied

- **Perinatal**: 16 weeks after fertilization to 30 days after birth
- **Elderly**: 60 or more years of age
- **Intermediate-age**: General population less than 60 years old, includes healthy people and people more susceptible to listeriosis
Risk Assessment Framework

Followed guidelines established by Codex Alimentarius, NACMCF, and ICMSF for the conduct of a microbial risk assessment:

- Transparency
- Broad scientific and stakeholder input
- Extensive peer review
Technical and Scientific Reviews of the FDA/FSIS Risk Assessment

Request for Data and Information
- Federal Register Notice
- Public Meetings
- Advisory Committee (NACMCF)

Internal and External Review
- Data and Assumptions
- Model
- Draft Document

Draft for Public Comment

Revised Document
Exposure Assessment

Number of *L. monocytogenes* ingested

- Frequency of contamination of food
- Extent of contamination
- Growth before consumption
- Frequency that food is consumed
- Amount of food consumed at a serving
The Real World

Home Refrigerator Temperatures (°F)
Hazard Characterization

- Probability of illness/mortality as a function of number of *L. monocytogenes* ingested
  - Dose-response curve “shape” from mice
  - Variation in virulence of *L. monocytogenes* isolates
  - Accounting for differences in susceptibility of mice and men - “anchor to health statistics”
  - Variation in susceptibility within age groups
  - Variation in susceptibility between age groups
Dose Response Curve – Elderly Population

Dose (Log10 cfu) vs. Mortality (Rate per Meal)
Risk Characterization

Combine exposure assessment and hazard characterization

- Frequency of death (mortality)
- Convert to severe cases of listeriosis by multiplying by 5

Characterize variability and uncertainty
Risk Characterization

Exposure assessment
- Number of Lm consumed per serving

Hazard characterization
- Dose-response model (mortality)

Mortality cases per serving

Frequency of servings

Listeriosis cases per annum

Listeriosis cases per serving

$\times 5$

Repeat 4,000 times!
Risk Characterization

Examined results in light of:

- Quantitative results
  - Data variability
  - Model uncertainty
- Consideration of qualitative factors
  - Epidemiological history
  - Food characteristics
- Extensive discussion of each food category
Listeriosis: Predicted Relative Risk per Serving—Total Population

The diagram shows the median predicted cases per 100 million servings for different food categories.
Listeriosis: Predicted Relative Risk per Annum
– Total Population

Median Cases per Annum

0
200
400
600
800
1000
1200
1400
1600

DM
PM
DS
FF
MD
SS
P
FS
CR
PC
V
DFS
PF
F
SC
UM
RS
GC
AC
IC
Initial Conclusions and Interpretation

Broad themes reemphasized:
- Disease primarily impacts specific “at-risk” subpopulations
- Disease is rare but severe
- Substantial difference in risk among different food categories
Initial Conclusions and Interpretation

Major factors that affect risk:
- Amount and frequency of consumption
- Frequency and levels of contamination
- Ability of food to support growth
- Refrigerated storage temperature
- Refrigerated storage time
Public comments

Submissions to the docket represented

- Consumer groups, industry, trade associations, expert modelers, manufacturers of food processing equipment, food retailers, marketers for food producers/processors, and education/scientific societies
Revised Risk Assessment

- Revise food categories
- Weighting of contamination data based on geography, year, and study size
- Add new exposure data
- Improved growth models
- Improved uncertainty analysis
Development of “What-If” Scenarios

Effect of Storage Time

Deli Meat - Elderly

Annual Mortality vs Maximum Storage Time (Days)
Summary: FDA/FSIS Risk Assessment

- The revised model is completed and undergoing scientific and management review.
- The revised risk assessment report is being prepared for scientific and organizational reviews.
- Answers questions on regulatory focus and research needs.
FAO/WHO Risk Assessment
Background

- Codex Alimentarius Committee on Food Hygiene (CCFH) developing guidance document on *Listeria monocytogenes*
- Considering different risk management options including the development of a Food Safety Objective
- Asked JEMRA (FAO/WHO) to conduct risk assessment
The *Listeria* “Problem”

CCFH posed three questions:

- What would be the impact of varying “criteria” between absence in 25 g to 1000 CFU per gram on the risk of listeriosis?
The *Listeria* “Problem”

CCFH posed three questions:

- What would be the impact of varying “criteria” between absence in 25 g to 1000 CFU per gram on the risk of listeriosis?
- What is the difference in risk associated with foods that do and do not support growth of *L. monocytogenes*?
The *Listeria* “Problem”

CCFH posed three questions:

- What would be the impact of varying “criteria” between absence in 25 g to 1000 CFU per gram on the risk of listeriosis?
- What is the difference in risk associated with foods that do and do not support growth of *L. monocytogenes*?
- What is the relative risk of listeriosis among different subpopulations as compared to the general population?
Approach

- Limited time and resources
- Complicated by international nature of risk assessment team
- Extensive hazard characterization with “simplified” dose response model
- Limited exposure assessment
- Used as basis for answering questions as simply as possible
Approach

Did complete quantitative risk ranking risk assessment but with four foods only
- Pasteurized milk
- Ice cream
- Smoked fish
- Fermented meats

Chosen to represent certain characteristics
Question 1: “Regulatory Criteria”

- Answered “simply” based on dose-response models developed in hazard characterization.
- Varied dose between 0.04 to 1000 CFU/g.
- Non-threshold model.
- Risk ≥ 25,000 fold higher at 1000 cfu/g compared with absence/25g.
- However.......
# Predicted Relationships Between Dose and Incidence

<table>
<thead>
<tr>
<th>Level of Lm in food at consumption</th>
<th>% servings annually at that level</th>
<th>% cases attributable to that level</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.04</td>
<td>96.37</td>
<td>0.02</td>
</tr>
<tr>
<td>0.1</td>
<td>1.90</td>
<td>&gt;0.01</td>
</tr>
<tr>
<td>1</td>
<td>0.91</td>
<td>0.01</td>
</tr>
<tr>
<td>10</td>
<td>0.43</td>
<td>0.03</td>
</tr>
<tr>
<td>100</td>
<td>0.21</td>
<td>0.13</td>
</tr>
<tr>
<td>1000</td>
<td>0.10</td>
<td>0.60</td>
</tr>
<tr>
<td>10,000</td>
<td>0.05</td>
<td>2.85</td>
</tr>
<tr>
<td>100,000</td>
<td>0.02</td>
<td>13.47</td>
</tr>
<tr>
<td>&gt;1,000,000</td>
<td>0.01</td>
<td>82.89</td>
</tr>
</tbody>
</table>


## Criteria: “Current Levels Scenario”

| Level (CFU/g) | Maximum Dose (CFU) | Percentage of servings when maximum dose | Estimated number of listeriosis cases per
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>0.04</td>
<td>1</td>
<td>100</td>
<td>0.3</td>
</tr>
<tr>
<td>0.1</td>
<td>3</td>
<td>3.6</td>
<td>0.4</td>
</tr>
<tr>
<td>1</td>
<td>32</td>
<td>1.7</td>
<td>0.5</td>
</tr>
<tr>
<td>10</td>
<td>316</td>
<td>0.8</td>
<td>1.3</td>
</tr>
<tr>
<td>100</td>
<td>3160</td>
<td>0.4</td>
<td>4.8</td>
</tr>
<tr>
<td>1000</td>
<td>31,600</td>
<td>0.2</td>
<td>21.6</td>
</tr>
</tbody>
</table>

Assumption: Distribution of *L. monocytogenes* levels as depicted in FDA/FSIS risk assessment, with no servings exceeding the maximum dose.
### Criteria: “Worst Case Scenario”

<table>
<thead>
<tr>
<th>Level (CFU/g)</th>
<th>Dose (CFU)</th>
<th>Probability of illness per serving</th>
<th>Estimated number of cases per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.1</td>
<td>3</td>
<td>$1.50 \times 10^{-11}$</td>
<td>1</td>
</tr>
<tr>
<td>1</td>
<td>32</td>
<td>$1.60 \times 10^{-10}$</td>
<td>10</td>
</tr>
<tr>
<td>10</td>
<td>316</td>
<td>$1.58 \times 10^{-9}$</td>
<td>101</td>
</tr>
<tr>
<td>100</td>
<td>3160</td>
<td>$1.58 \times 10^{-8}$</td>
<td>1,013</td>
</tr>
<tr>
<td>1000</td>
<td>31,600</td>
<td>$1.58 \times 10^{-7}$</td>
<td>10,128</td>
</tr>
</tbody>
</table>

Assumption: All servings at dose indicated and no servings exceed this value.
Role of Compliance

<table>
<thead>
<tr>
<th>% Defectives (10^6 CFU/g)</th>
<th>Criteria: 0.04 CFU/g</th>
<th>Criteria: 100 CFU/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.000000</td>
<td>0.5*</td>
<td>5.7</td>
</tr>
<tr>
<td>0.000001</td>
<td>1.7</td>
<td>6.9</td>
</tr>
<tr>
<td>0.000100</td>
<td>12.3</td>
<td>17.4</td>
</tr>
<tr>
<td>0.001000</td>
<td>119</td>
<td>124</td>
</tr>
<tr>
<td>0.010000</td>
<td>1,185</td>
<td>1,191</td>
</tr>
<tr>
<td>0.018000</td>
<td>2,133</td>
<td>2,133</td>
</tr>
<tr>
<td>0.100000</td>
<td>11,837</td>
<td>11,848</td>
</tr>
<tr>
<td>1.000000</td>
<td>117,300</td>
<td>117,363</td>
</tr>
</tbody>
</table>

* Annual cases
Question 2: Increase in Risk Due to Growth

- **Milk**
  - Rarely contaminated, allows growth, high consumption

- **Ice cream**
  - Rarely contaminated, does not allow growth, high consumption

- **Smoked fish**
  - Often contaminated, allows growth, low consumption

- **Fermented meat**
  - Often contaminated, does not allow growth, low consumption
### Question 2: Increase in Risk Due to Growth

<table>
<thead>
<tr>
<th>Food</th>
<th>Cases per 100,000 people</th>
<th>Cases per 1,000,000 servings</th>
</tr>
</thead>
<tbody>
<tr>
<td>Milk</td>
<td>0.0910000</td>
<td>0.0050000</td>
</tr>
<tr>
<td>Ice Cream</td>
<td>0.0001200</td>
<td>0.0000140</td>
</tr>
<tr>
<td>Smoked Fish</td>
<td>0.0046000</td>
<td>0.0210000</td>
</tr>
<tr>
<td>Fermented Meats</td>
<td>0.0000066</td>
<td>0.0000025</td>
</tr>
</tbody>
</table>
Question 3: Relative Susceptibility

- Developed a quantitative approach based on dose-response model, and developed relative susceptibility values.

- Based on extensive epidemiological data available from France and United States.
# Key Findings: Relative Susceptibility

<table>
<thead>
<tr>
<th>Condition</th>
<th>Relative susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplant</td>
<td>2584</td>
</tr>
<tr>
<td>AIDS</td>
<td>865</td>
</tr>
<tr>
<td>Dialysis</td>
<td>476</td>
</tr>
<tr>
<td>Cancer-Pulmonary</td>
<td>229</td>
</tr>
<tr>
<td>Cancer-Bladder and prostate</td>
<td>112</td>
</tr>
<tr>
<td>Cancer-Gynaecological</td>
<td>66</td>
</tr>
<tr>
<td>Cancer-Blood</td>
<td>1364</td>
</tr>
<tr>
<td>Cancer-Gastrointestinal and liver</td>
<td>211</td>
</tr>
<tr>
<td>Non-cancer liver disease</td>
<td>143</td>
</tr>
<tr>
<td>Diabetes, non-insulin dependent</td>
<td>25</td>
</tr>
<tr>
<td>Diabetes, insulin dependent</td>
<td>30</td>
</tr>
<tr>
<td>Alcoholism</td>
<td>18</td>
</tr>
<tr>
<td>Over 65 years old</td>
<td>8</td>
</tr>
<tr>
<td>Less than 65 years, no other condition</td>
<td>1</td>
</tr>
</tbody>
</table>
Summary: FAO/WHO Risk Assessment

- Developed a quantitative risk assessment built on the concepts of the FDA/FSIS assessment, but focused on a somewhat simpler evaluation
- Successfully addressed CCFH questions
- Full document in final editing after international peer review.
Lessons Learned

- Substantial differences in the two risk assessments
- Reflect successfully responding to the management questions asked of the risk assessment teams
- Scientifically support each other while providing unique insights
- Need the flexibility to take different approaches