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

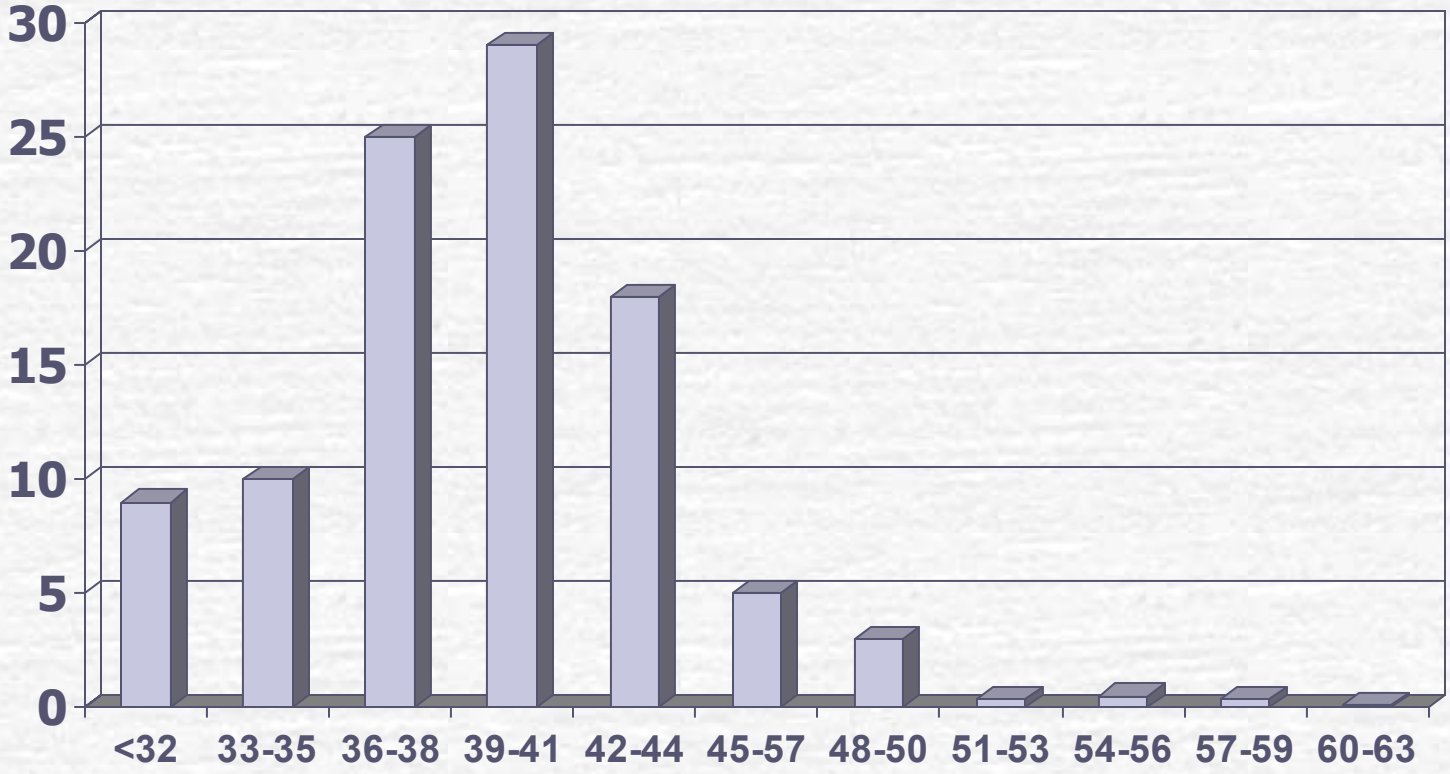
Draft for Public Comment

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

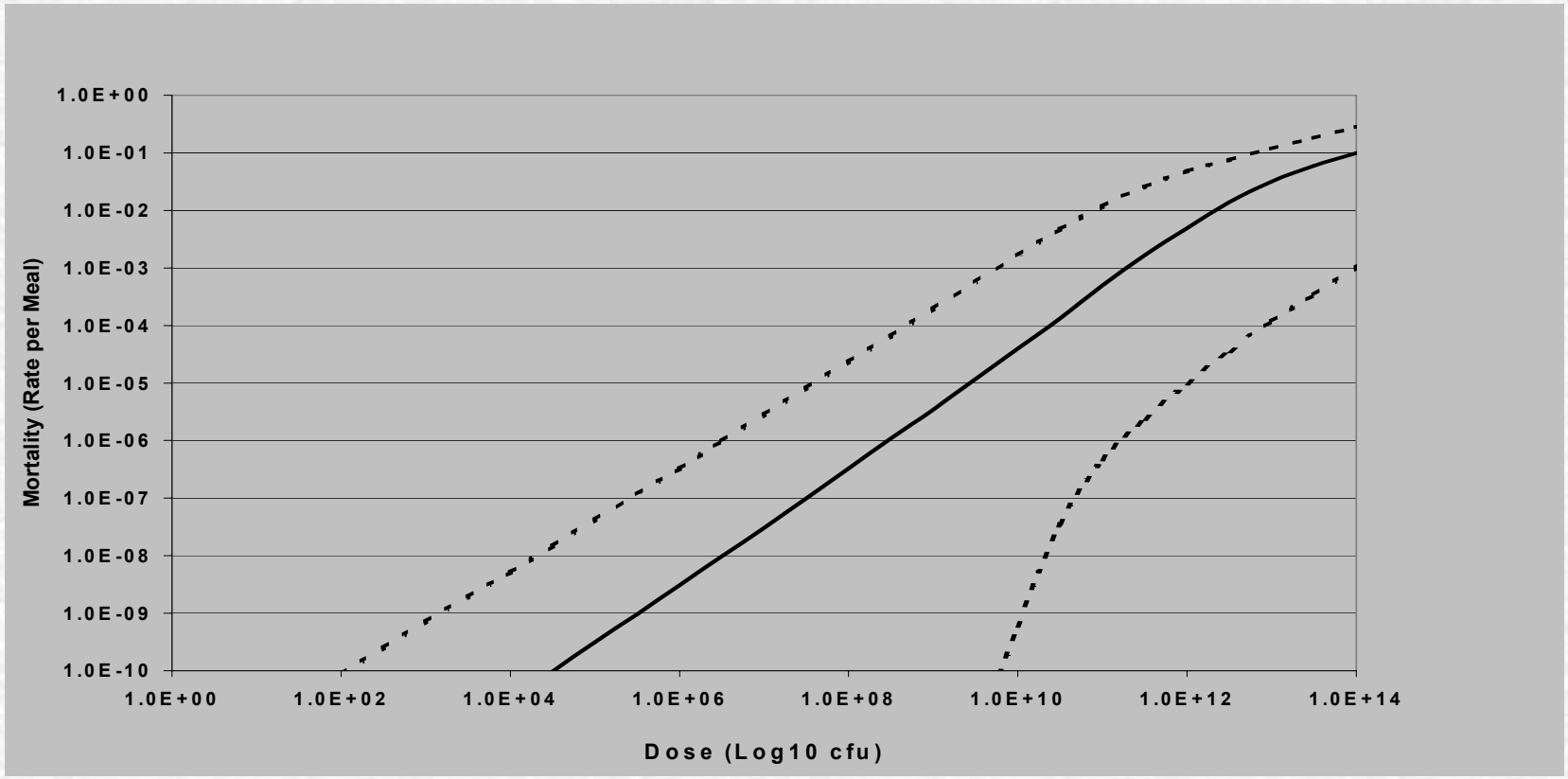


Home Refrigerator Temperatures (°F)

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



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)

[30,000 + 300] iterations

Mortality cases per serving

Frequency of servings

X 5

Listeriosis cases per annum

X 5

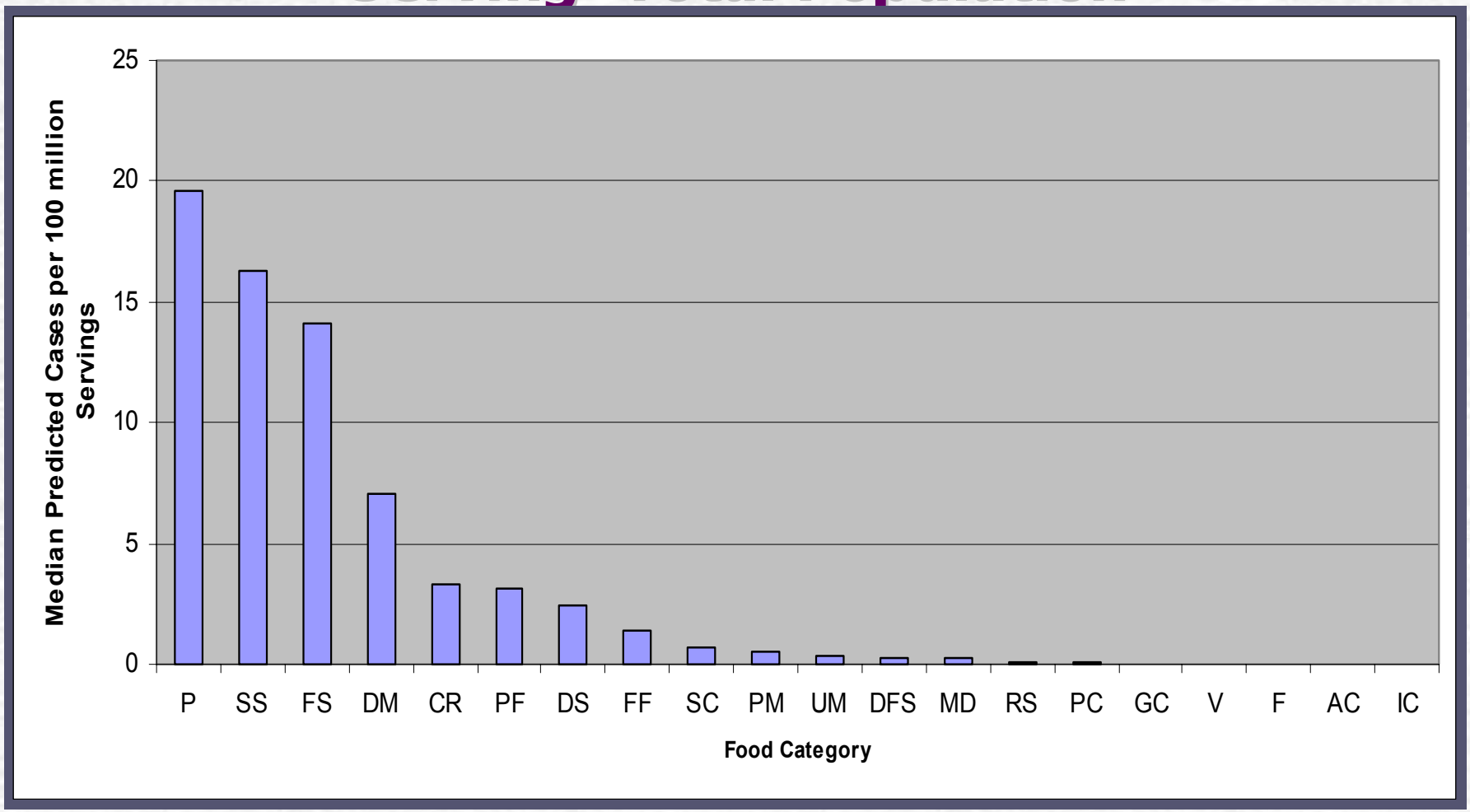
Listeriosis cases per serving

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



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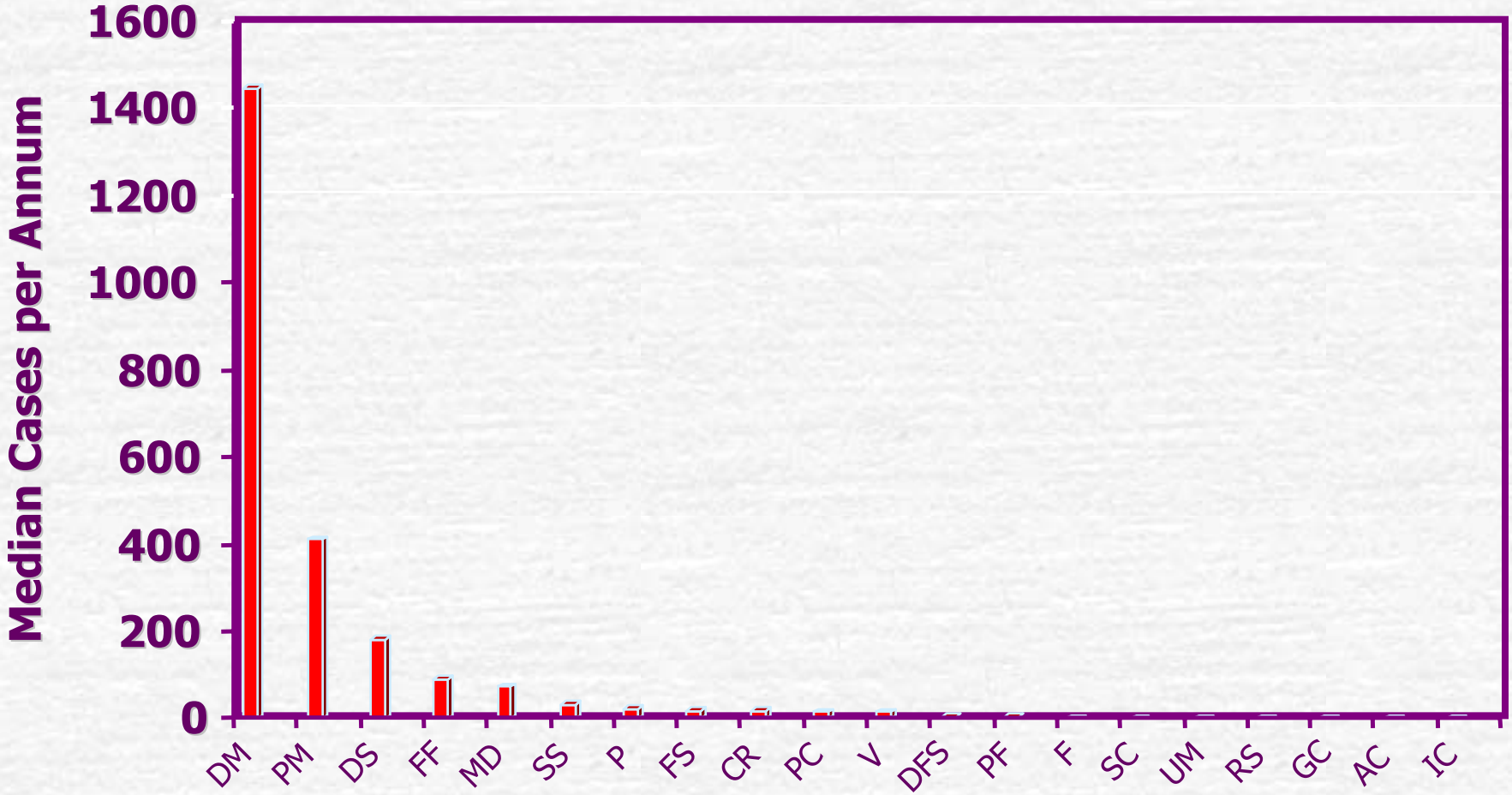


Initial Conclusions and Interpretation

- **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

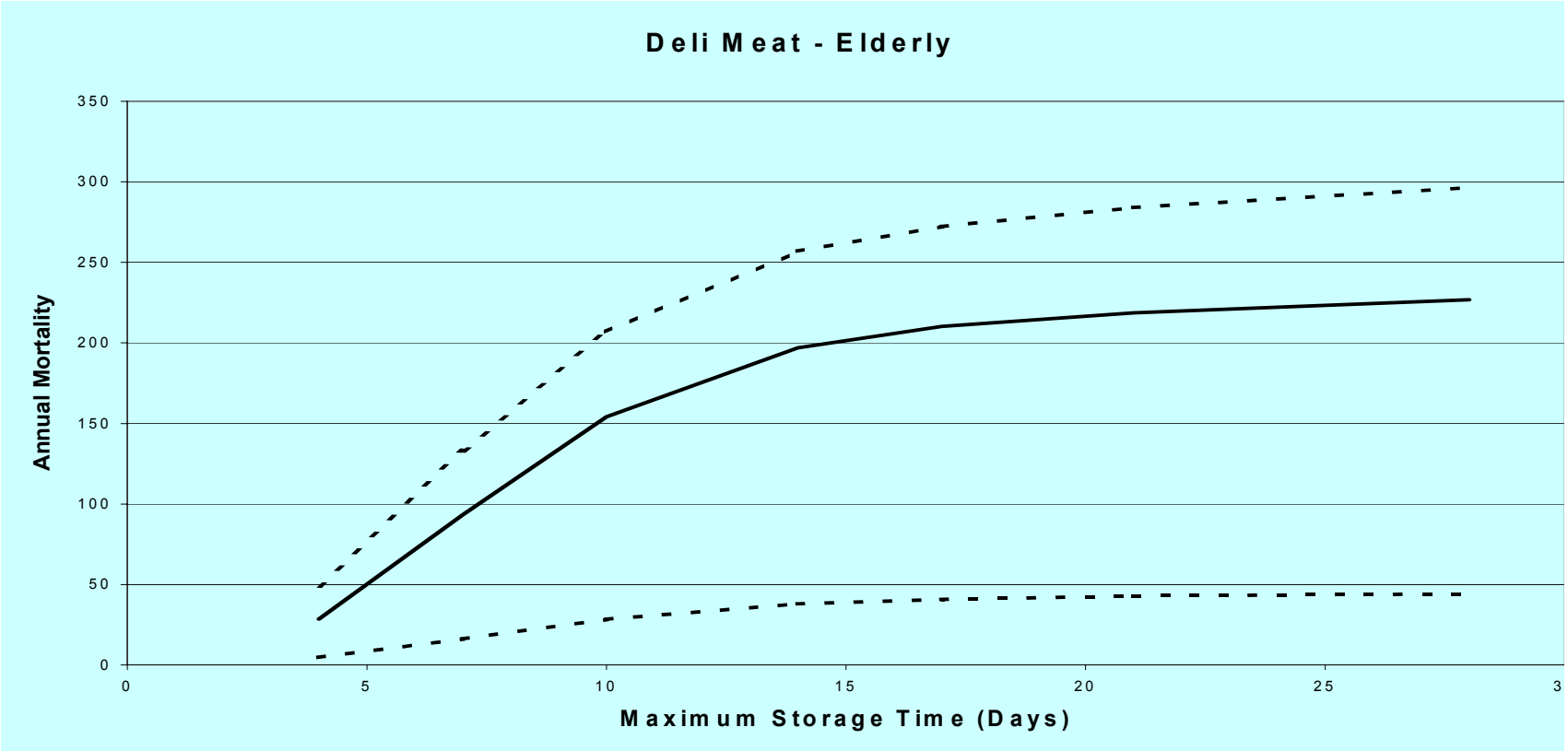
Public comments

- 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

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?

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- **CCFH posed three questions:**
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  - **What is the difference in risk associated with foods that do and do not support growth of *L. monocytogenes*?**

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- **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

Level of Lm in food at consumption	% servings annually at that level	% cases attributable to that level
0.04	96.37	0.02
0.1	1.90	>0.01
1	0.91	0.01
10	0.43	0.03
100	0.21	0.13
1000	0.10	0.60
10,000	0.05	2.85
100,000	0.02	13.47
>1,000,000	0.01	82.89

Criteria: "Current Levels Scenario"

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

Assumption: Distribution of *L. monocytogenes* levels as depicted in FDA/FSIS risk assessment, with no servings exceeding the maximum dose.

Criteria: "Worst Case Scenario"

Level (CFU/g)	Dose (CFU)	Probability of illness per serving	Estimated number of cases per year
0.1	3	1.50×10^{-11}	1
1	32	1.60×10^{-10}	10
10	316	1.58×10^{-9}	101
100	3160	1.58×10^{-8}	1,013
1000	31,600	1.58×10^{-7}	10,128

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

Role of Compliance

% Defectives (10^6 CFU/g)	Criteria: 0.04 CFU/g	Criteria: 100 CFU/g
0.00000	0.5*	5.7
0.00001	1.7	6.9
0.00010	12.3	17.4
0.00100	119	124
0.01000	1,185	1,191
0.01800	2,133	2,133
0.10000	11,837	11,848
1.00000	117,300	117,363

* 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

Food	Cases per 100,000 people	Cases per 1,000,000 servings
Milk	0.0910000	0.0050000
Ice Cream	0.0001200	0.0000140
Smoked Fish	0.0046000	0.0210000
Fermented Meats	0.0000066	0.0000025

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

Condition	Relative susceptibility
Transplant	2584
AIDS	865
Dialysis	476
Cancer-Pulmonary	229
Cancer-Bladder and prostate	112
Cancer-Gynaecological	66
Cancer-Blood	1364
Cancer-Gastrointestinal and liver	211
Non-cancer liver disease	143
Diabetes, non-insulin dependent	25
Diabetes, insulin dependent	30
Alcoholism	18
Over 65 years old	8
Less than 65 years, no other condition	1

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