微生物学的リスク評価
事例紹介

平成１７年9月６日

食品安全委員会

微生物･ウイルス合同専門調査会

専門委員　春日文子

リスク評価の流れ（例）

Exposure Assessment

使用するデータの例

収穫

収獲地での汚染実態

- 汚染率
- 汚染濃度
- 季節変動
- 地域差

輸送

（輸送中の増加）

- 時間・温度
- 輸送経路
- 予測微生物学的モデル

市場取引

市場での汚染実態

- 搬入時間・温度
- 予測微生物学的モデル

搬入

調理場搬入時の汚染実態

- 調理方法データ
- 予測微生物学的モデル

調理

調理後の汚染実態

- 消費量・摂食頻度データ

Hazard Characterization

摂取

ハザード
摂食頻度・量

用量－反応評価

用量－反応データ（宿主集団、ハザード、濃度、汚染食品喫食量、発症率、など）

回帰関数

罹患・発症

リスク総合評価

Risk Characterization

Draft Risk Assessment on *Vibrio parahaemolyticus* in Oysters

from the slides by
Marianne Miliotis, Ph.D.

for

UJNR Symposium March 2002

Tokyo, Japan

Food and Drug Administration
Center for Food Safety and Applied Nutrition

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タスクフォースメンバー構成

- **Team Leaders:**
  Marianne Miliotis, William Watkins
- **Harvest:**
  Marleen Wekell (Lead), Atin Datta, Elisa Elliot, Walter Hill, Charles Kaysner, Brett Podoski
- **Post Harvest:**
  Angelo DePaola, David Cook (Co-leads), George Hoskin, Susan McCarthy, William Watkins
- **Public Health:** John Bowers (Lead)
- **Epidemiology:**
  Marianne Ross (Segment lead), Karl Klontz, Debra Street, Babgaleh Timbo
- **Consumption:**
  Michael DiNovi
- **Dose-Response:**
  Donald Burr (Segment lead), John Bowers, Mahendra Kothary, Wesley Long, Marianne Miliotis, Ben Tall, Mark Walderhaug
- **Modeling:**
  John Bowers (Lead), Mark Walderhaug

この他に多数の助言者、情報提供者等の協力者

リスク評価手順の概要
(FDAによる腸炎ビブリオリスク評価の場合)

- 背景
- 目的
- 範囲
- アプローチの説明
- 導入した仮定
- 結果
- まとめ

目的

- Produce a **mathematical model** to predict the **estimated incidence** of illness incurred by consumers of **raw oysters** containing pathogenic *Vp*
- **Provide FDA with information** that will assist the agency with the review of current **programs** relating to regulatory and guidance issues for *Vp* in raw molluscan shellfish to ensure that such programs protect the public health

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範囲

- Assess human exposure to pathogenic *Vp* via consumption of raw oysters
- Determine the relationship between levels of *Vp* in raw oysters and illness
- Estimate the number and severity of sporadic cases of illness associated with the level of *Vp* consumed by healthy and immune compromised subpopulations

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範囲

- Evaluate the potential effectiveness of preventive and intervention strategies
- Evaluate the effectiveness of FDA's previous guideline of no more than 10,000 *Vp*/g in raw oysters
- Provide a tool to evaluate criteria for *Vp* for opening and closing shellfish waters for commercial harvesting

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Risk Assessment Process

- **Hazard Identification**
  - Pathogenic *Vp* in raw molluscan shellfish
- **Exposure Assessment**
  - Determination of the likelihood of ingesting *Vp* by eating raw molluscan shellfish harboring the organism
- **Hazard Characterization / Dose-Response**
  - Relationship of the levels of *Vp* ingested with the frequency and magnitude of illness
- **Risk Characterization**
  - Integration of hazard characterization and exposure assessment to determine the risk of illness

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Risk Assessment Approach
Exposure Assessment

Harvest

Post Harvest

Consumption

Spring

Summer

Fall

Winter

Pacific NW
Mid Atlantic
Atlantic NE
LA GULF
nonLA GULF

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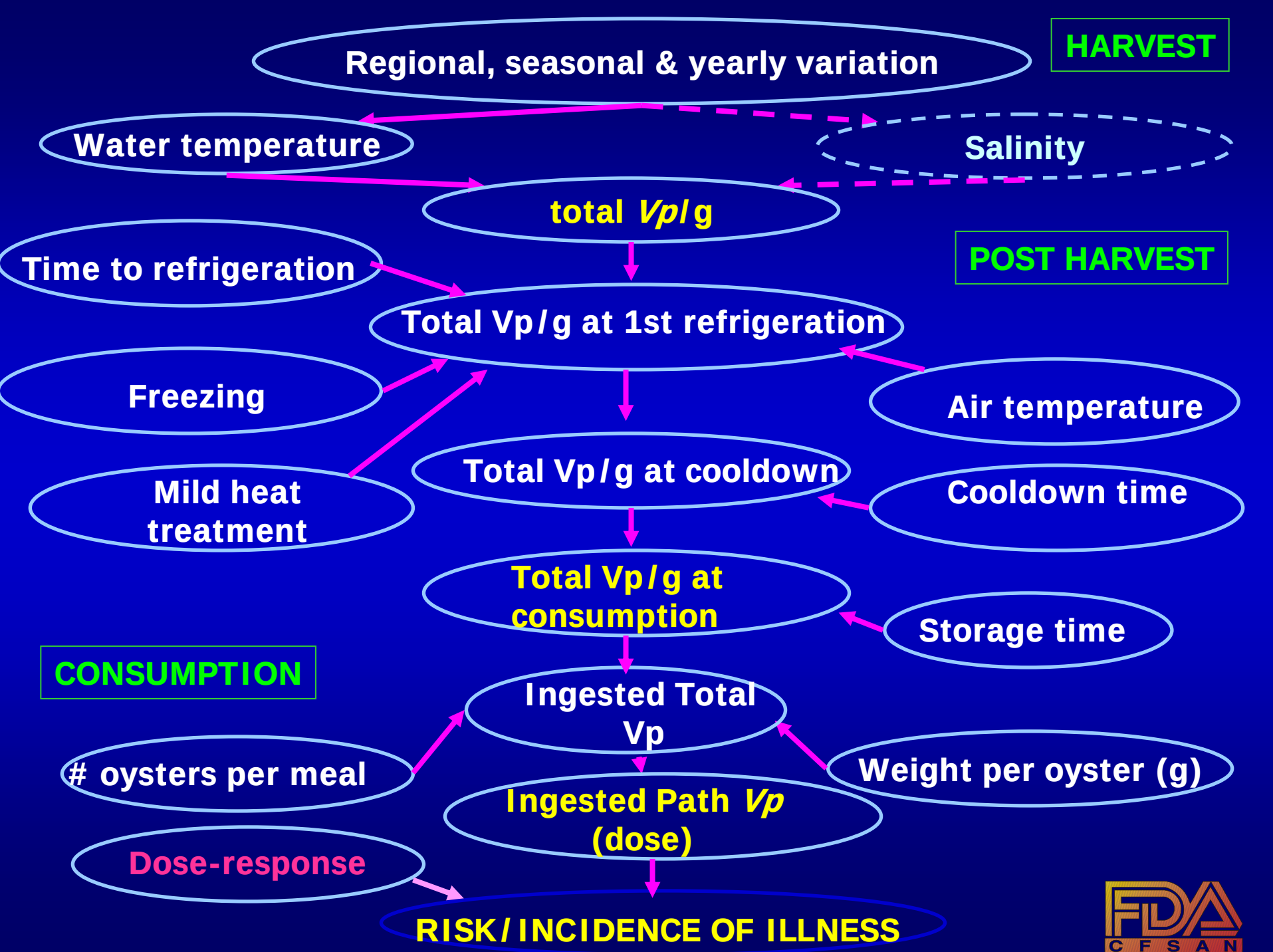
HARVEST
Regional, seasonal & yearly variation
Water temperature
Salinity
total Vp/g
POST HARVEST
Time to refrigeration
Total Vp/g at 1st refrigeration
Freezing
Air temperature
Total Vp/g at cooldown
Mild heat treatment
Cooldown time
Total Vp/g at consumption
Storage time
CONSUMPTION
Ingested Total Vp
oysters per meal
Weight per oyster (g)
Ingested Path Vp (dose)
Dose-response
RISK/INCIDENCE OF ILLNESS
FDA
CFSAN

仮定

- Pathogenesis was based on the presence of the most characterized virulence factor of the organism, thermostable direct hemolysin (TDH)
- Equal virulence was assumed for all pathogenic *Vp*
- All *Vp* in oysters, regardless of pathogenicity, have similar growth and survival rates
- Lag time to growth of *Vp* in oysters after harvest is negligible

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仮定

- The growth rate of *Vp* in oysters is approximately 1/4 of the growth rate observed in laboratory experimentation
- The growth rate of *Vp* drops uniformly down to zero during the period of initial refrigeration following harvest
- Oyster landings and consumption data were used to estimate the illnesses attributable to the region where oysters originated

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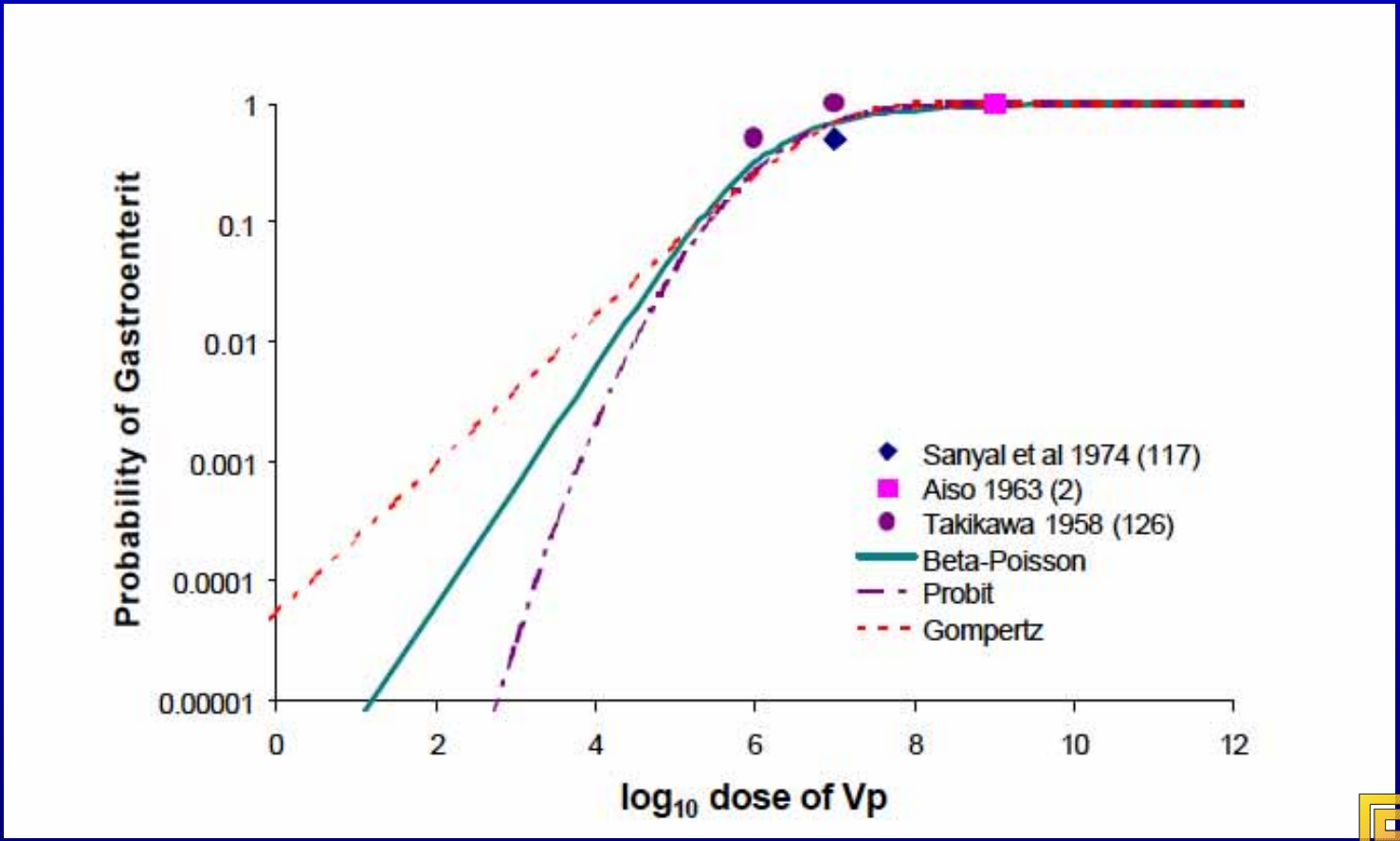
Maximum likelihood estimates (MLE) of the Beta-Poisson, Gompertz, and Probit dose-response curves based on pooled data from human feeding studies of *V. parahaemolyticus* (Vp)



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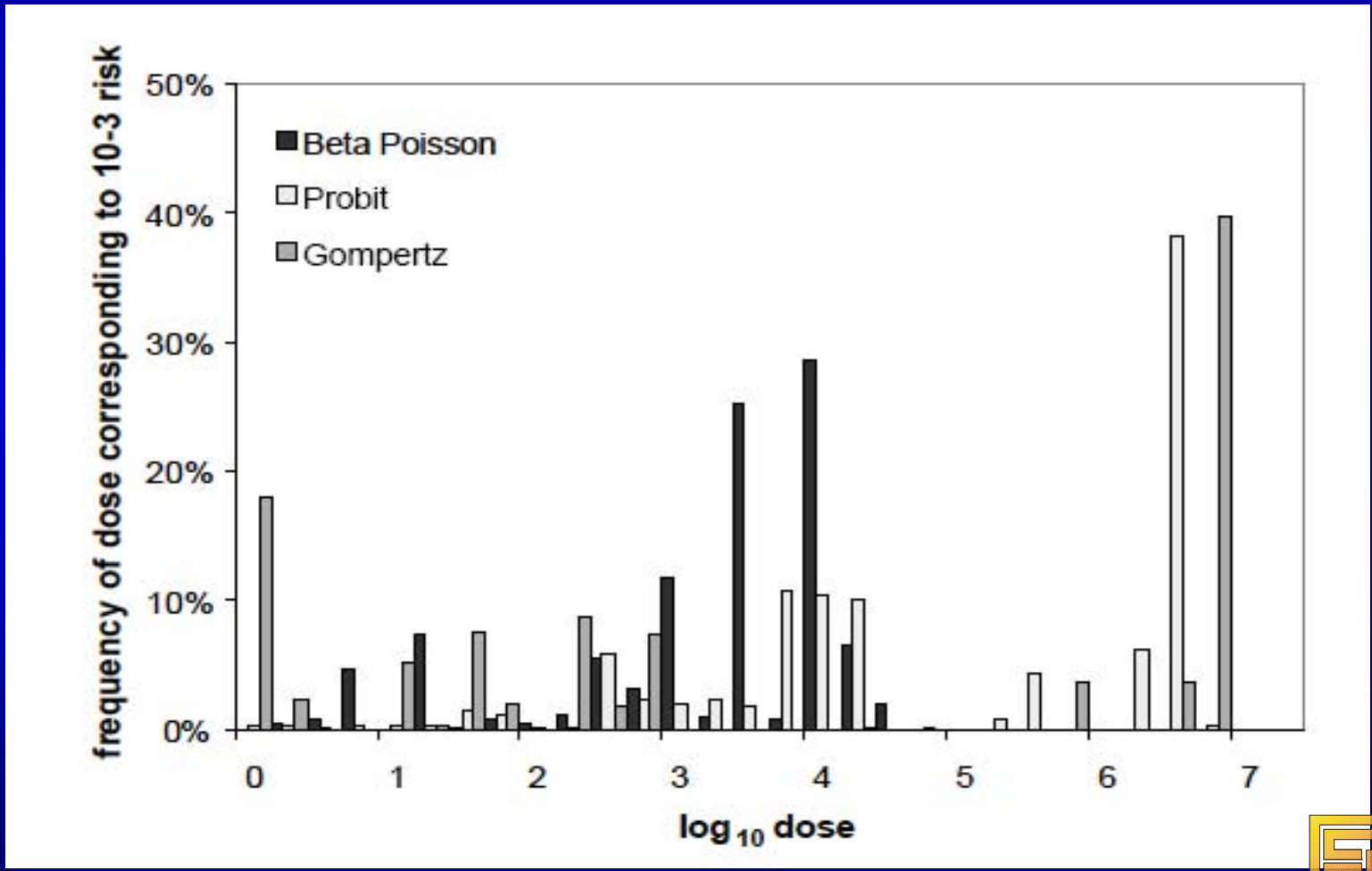
Uncertainty distribution of infectious dose of *V. parahaemolyticus* corresponding to 10-3 risk for Beta-Poisson, Gompertz, and Probit dose response models



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Case Series Statistics (CDC data)

- 107 oyster-related culture-confirmed *V. parahaemolyticus* cases (sporadic- and outbreak-related) occurring during 1997 and 1998 in the Gulf Coast States :
  - 5 septicemia
  - 1 death
  - Of cases with available information:
    - 23 of 79 (29%) cases occurred in individuals with underlying chronic conditions
    - 27 of 90 (30%) gastroenteritis cases were hospitalized
    - 3 of 4 (75%) septicemia cases had an underlying chronic condition

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リスク評価結果の内容
(FDAによる腸炎ビブリオリスク評価の場合)

- 季節、産地海域ごとの散発事例患者数の発生推定数
- 感度分析 (どの要因が結果に大きく影響しているか)
- 対策効果の推定 (基準値の違いも含む)
- 不確実性分析
- 用量反応評価における回帰モデルの違いの分析
- リスク評価結果の検証

Sporadic Illnesses predicted by the *V. parahaemolyticus* Risk Assessment

Region / Season	Fall	Winter	Spring	Summer
Gulf Coast	400	25	1,200	3,000
Mid-Atlantic	ND	ND	10	12
Pacific NW	ND	ND	15	50
Atlantic NE	ND	ND	12	30

ND - Not determinable

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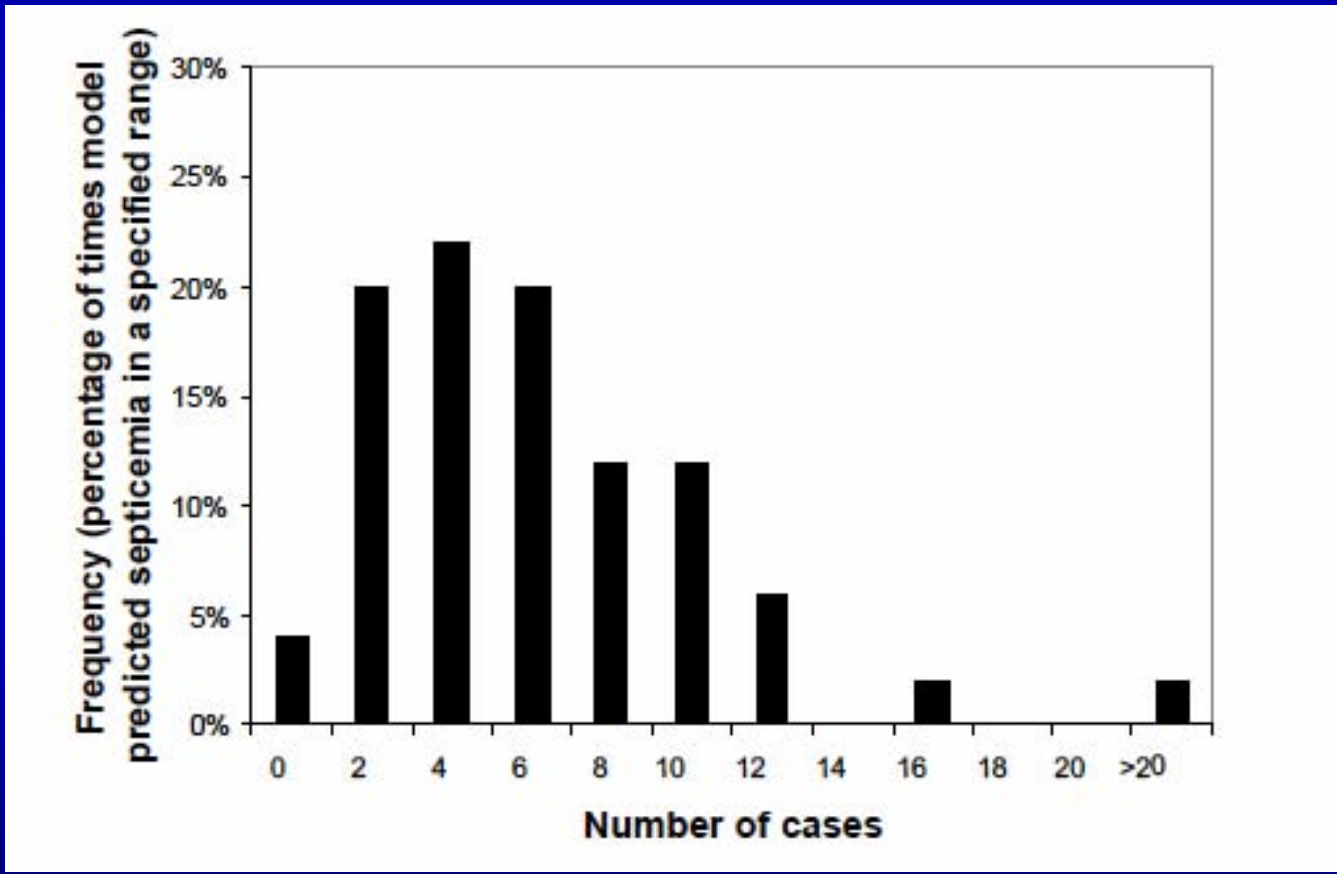
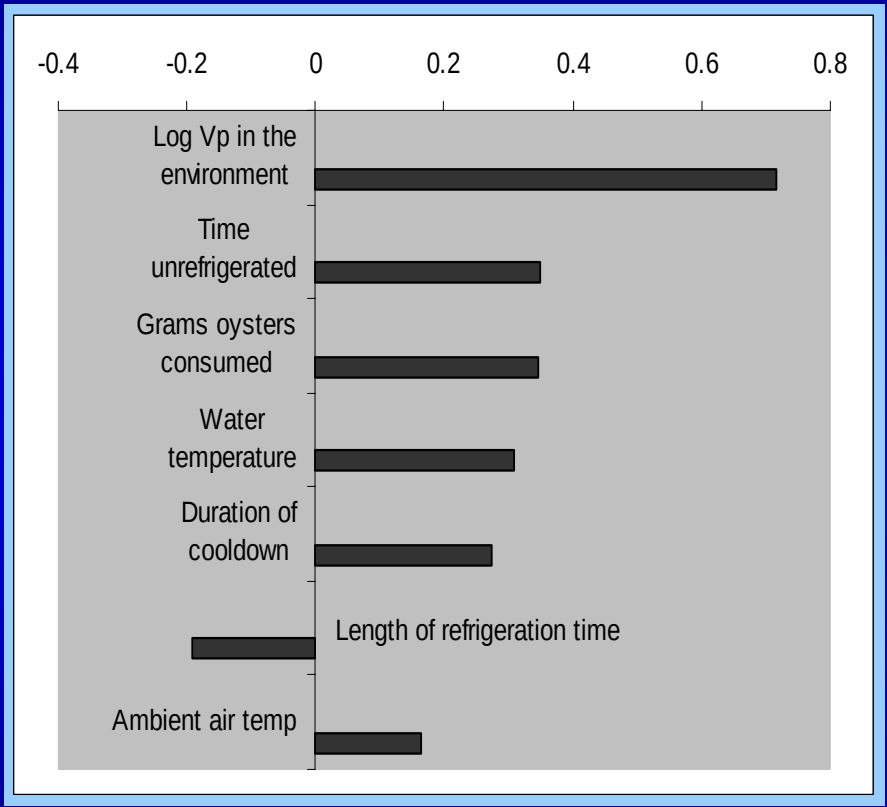
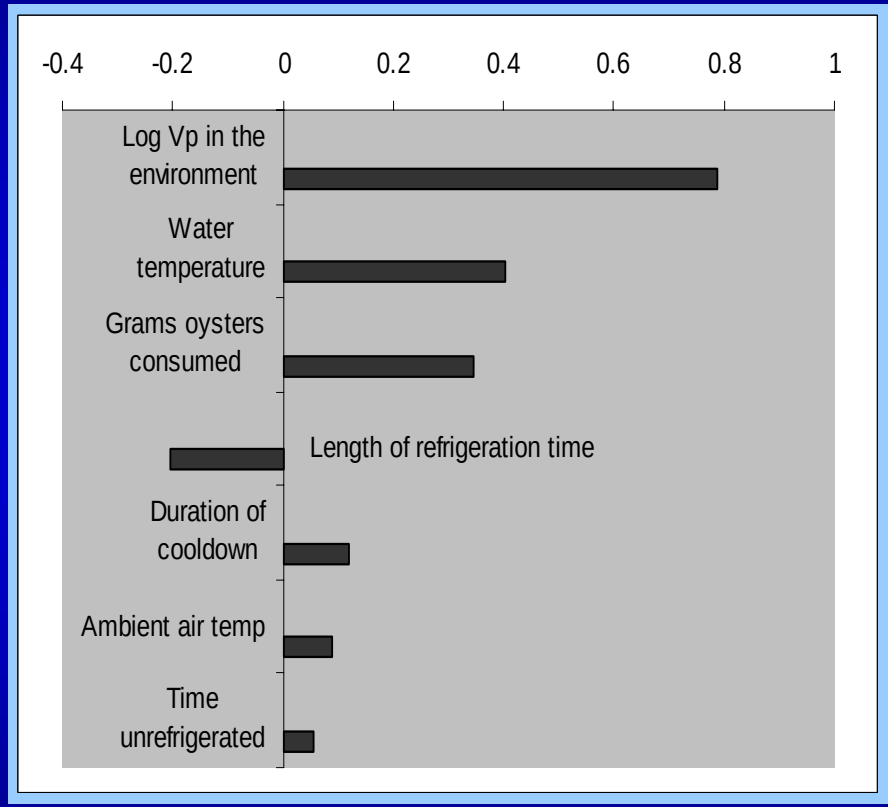
Distribution of probable number of cases of *V. parahaemolyticus*-associated cases of septicemia occurring per year (all seasons and regions)



感度分析



ルイジアナ州以外のメキシコ湾岸



北西太平洋岸

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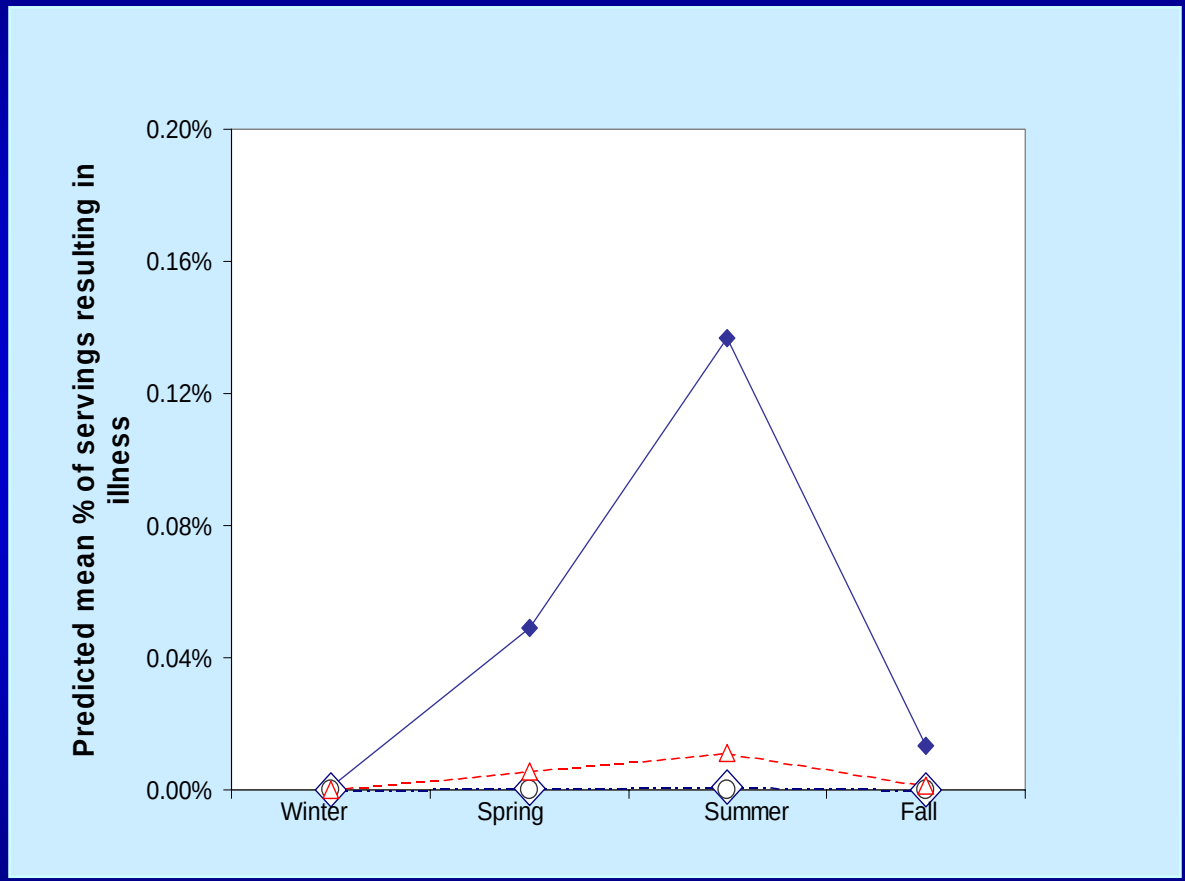
可能な対策の効果の比較



Effect of intervention measures on reducing the predicted risk of *V. parahaemolyticus* illnesses from Gulf Coast summer harvest: no mitigation (♦); freezing (◊); heat treatment (□); rapid cooling (∈).

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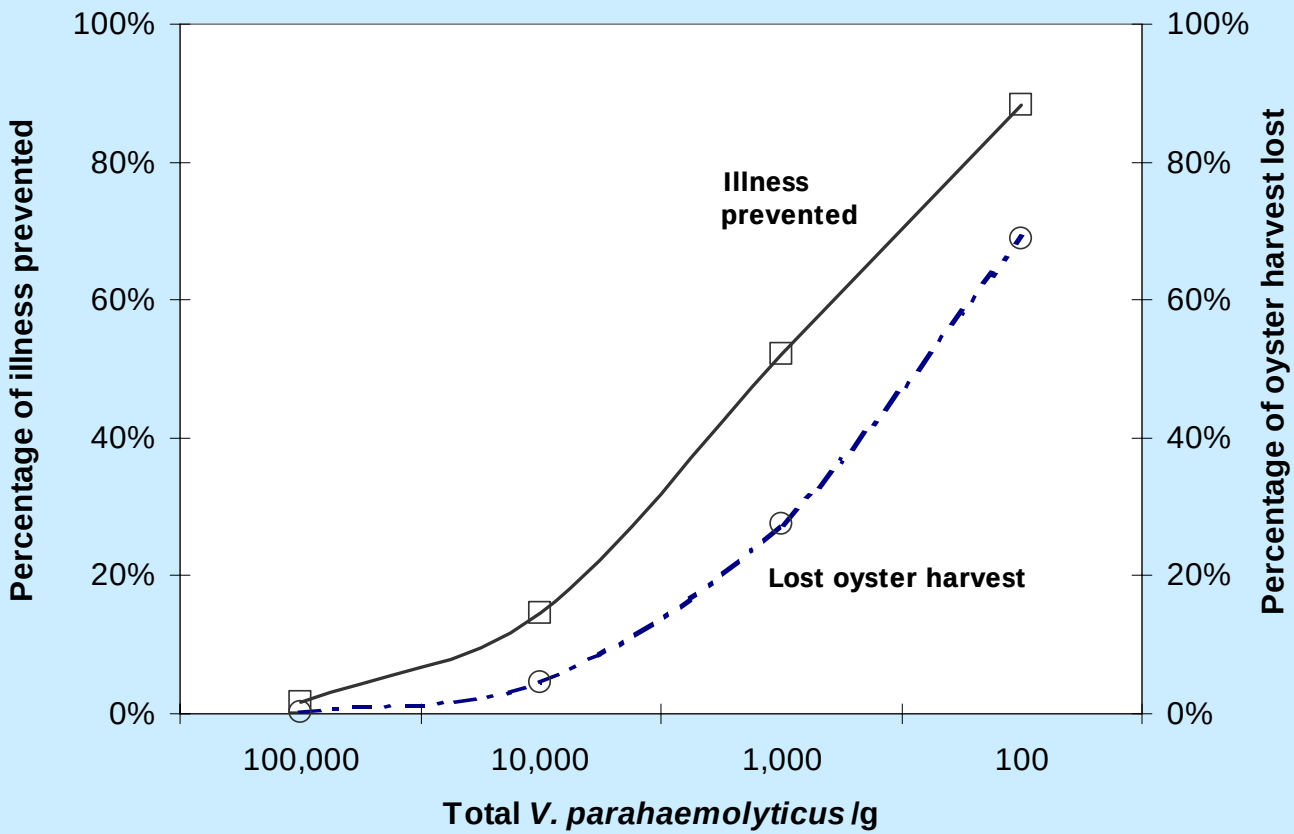
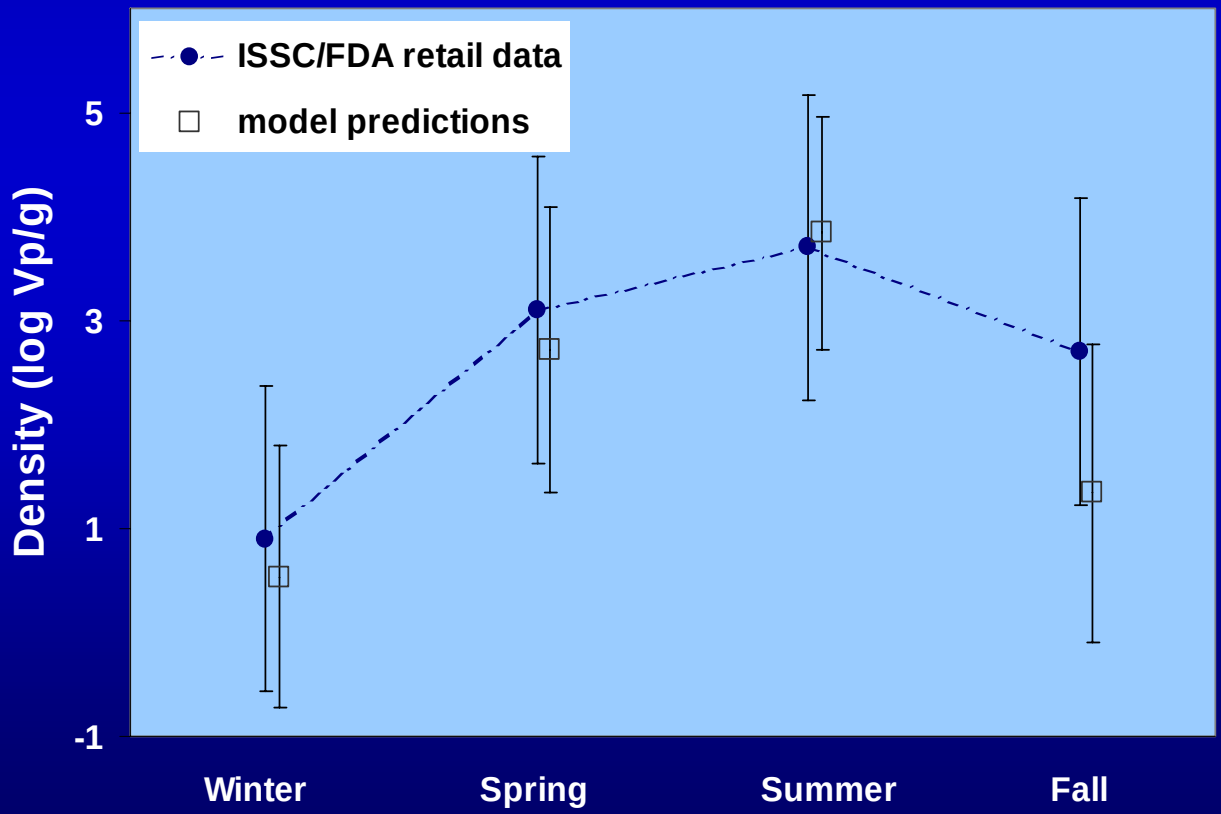
収獲段階における総 Vp / g 規制値による効果



リスク評価モデルの検証

小売店での汚染実態調査データ

vs モデルによる予測データ



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Enterobacter sakazakii and other microorganisms in powdered infant formula

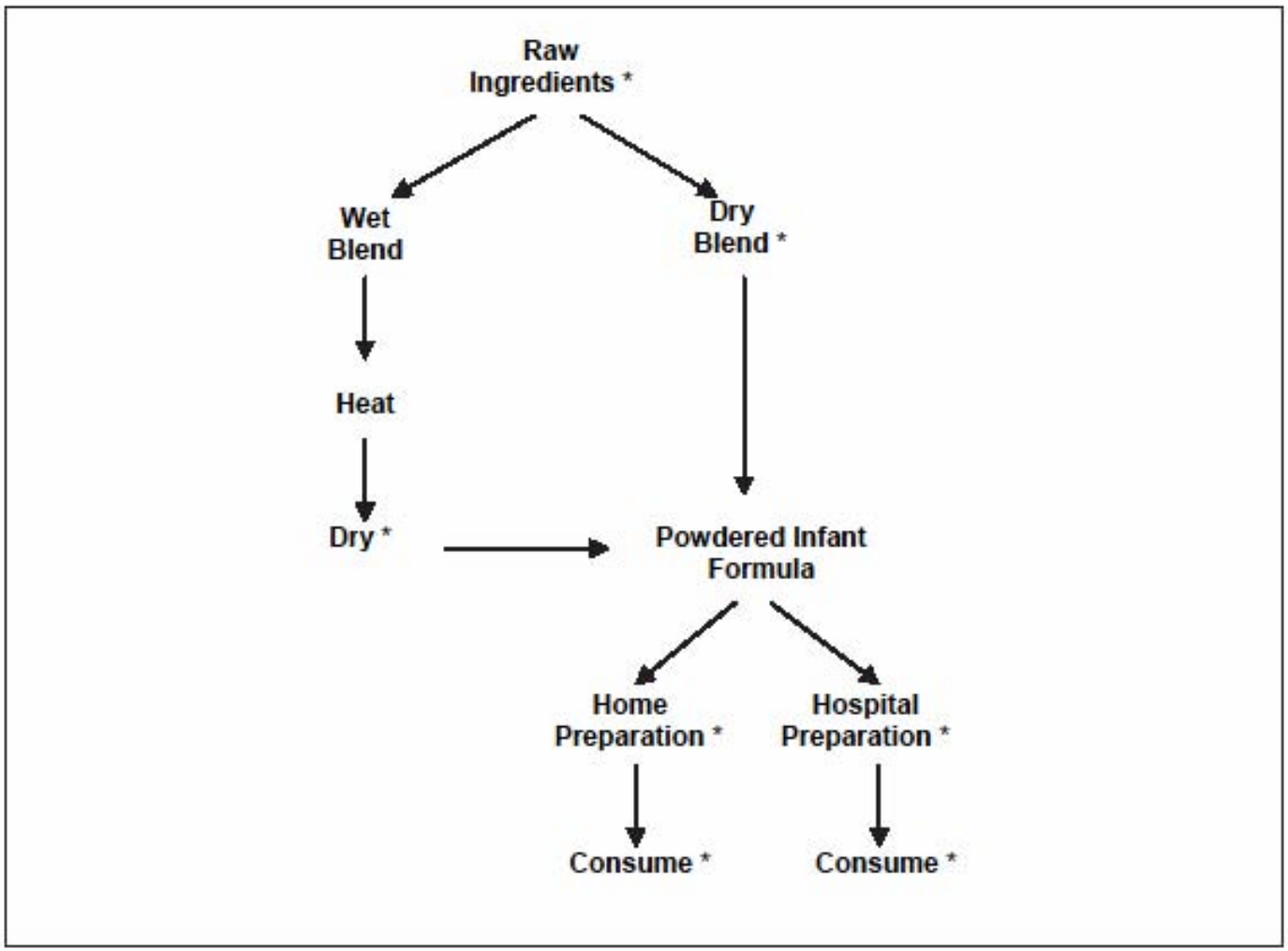
FAO/WHO

MRA Series No. 6

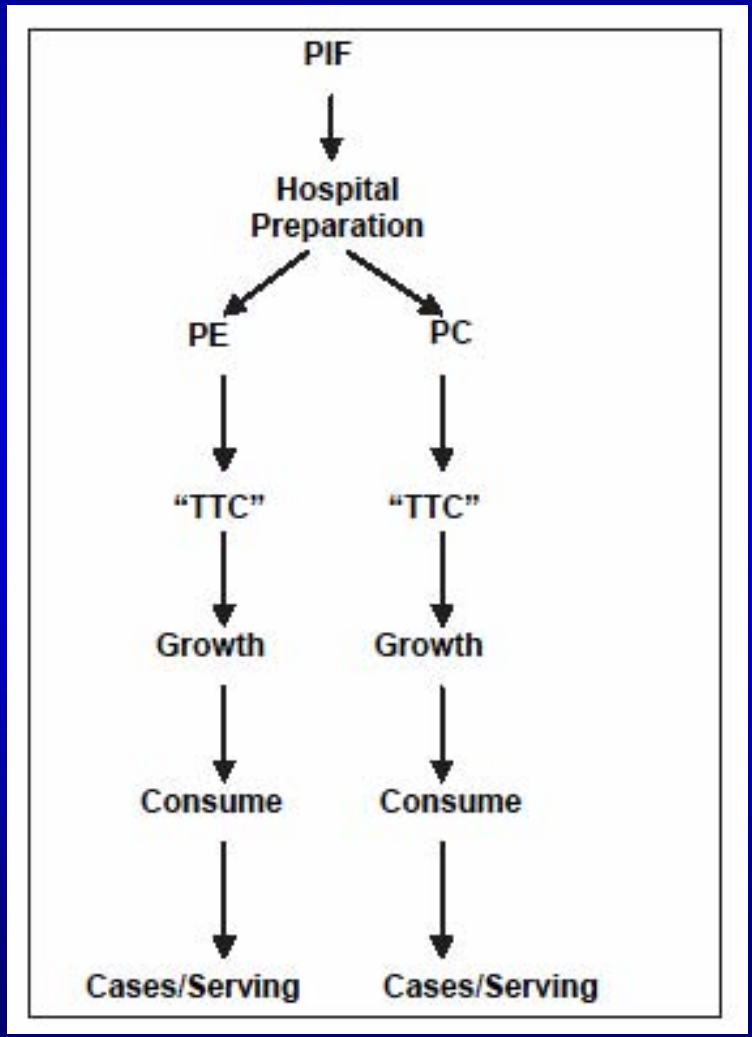
リスク評価の目的：
以下の4つの質問に対して回答すること

- What are the factors that contribute to the microbial food safety risks associated with powdered infant formula and what is their relative importance?
- What are potential interventions that could mitigate these risks, and what is the relative efficacy of those interventions?
- What key scientific knowledge and/or data are needed to reduce the uncertainty associated with the estimates of risks and the estimates of the relative effectiveness of identified risk control options?
- What are potential consequences associated with the identified risk control options if implemented?

乳児用粉ミルクの製造工程（模式図）



リスク評価モデルの流れ図



PIF: Powdered Infant Formula
PE: Contamination from the preparation environment
PC: Contamination from the infant formula
TTC: Time to consumption

*E. Sakazakii*と*S. enterica*を対象

専門家会議報告におけるシンプルなリスク評価

特定の仮定条件におけるシンプルモデルを用いた“what-if” シナリオ

以下のシナリオにおける**相対リスク**を算出（*E. Sakazaki*）

- シナリオ1：粉ミルクの汚染頻度の違い
- シナリオ2：調乳後ミルク消費までの時間
- シナリオ3：調乳後のミルクの環境からの汚染の頻度
- シナリオ4：乳児の感受性の差異
- シナリオ5：調乳後処理（高温湯での調乳、再加熱など）
- シナリオ6：複数のシナリオの組み合わせ