USDA

United States Department of Agriculture

One Team, One Purpose

Food Safety and Inspection Service

Protecting Public Health and Preventing Foodborne Illness

Summary from IRAC Workshop

Advances in WGS and the Implications on the Conduct and Application of Risk Assessment in Food Safety Decision-Making

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International Association for Food Protection Conference
Salt Lake City, UT – July 11, 2018

Presentation Overview

- Interagency Risk Assessment Consortium (IRAC)
- 2017 IRAC Workshop: Application of WGS to Assess Food Safety Risk
  - Objectives, Process & Findings
- Next Steps: Interagency Action Plan

IRAC's Role

Coordinates Federal agencies efforts & ensures communication that develop or use food safety risk assessments

Comprehensive view of existing and emerging public health needs for risk assessment

Streamlines and creates synergies:

Information sharing about methods, projects, research needs, events & opportunities

Opportunities for collaboration & solutions

Work Group & Objectives

Implications of WGS for quantitative microbiological risk assessment (QMRA)

- hazard identification
- exposure assessment
- hazard characterization
- risk characterization

Opportunities and challenges in using WGS to advance QMRA

Implications of applying WGS to QMRA in regulatory decision-making

Member Agencies:

- **Department of Agriculture**
  - Agricultural Marketing Service
  - **Agricultural Research Service**
  - **Animal and Plant Health Inspection Service**
  - Economic Research Service
  - Food and Nutrition Service
  - **Food Safety and Inspection Service**
  - National Agricultural Statistics Service
  - **National Institute of Food and Agriculture**
  - **Office of the Chief Scientist**
  - Office of Pest Management Policy*
  - Office of Risk Assessment and Cost Benefit Analysis
- **Department of Commerce**
  - National Oceanic and Atmospheric Administration
- **Department of Health and Human Services**
  - Centers for Disease Control and Prevention
    - **National Center for Emerging and Zoonotic Infectious Diseases**
    - **National Institute for Occupational Safety and Health**
  - Food and Drug Administration
    - **Center for Food Safety and Applied Nutrition**
    - Center for Veterinary Medicine
    - **Office of Foods and Veterinary Medicine**
  - **National Inst. of Health, Natl. Institute of Allergy and Infectious Dis.**
- **Environmental Protection Agency**
  - Office of Pesticide Programs
  - Office of Water
- **U.S. Agency for International Development**

Work Group Process

1. Review of the Scientific Literature
- 33 scientific articles (Foodrisk.org)

2. Educational Webinars
- Overview & Transformation of surveillance & outbreak investigations (Williams/Allard/Brown)
- WGS: What epidemiologists need to know (Wiedmann)
- WGS/QMRA (Havelaar/Wasserman); WGS/AMR (Zagmutt/Morley)

3. In-Depth Interagency Discussions
- 12 meetings total
- Oral and written responses to core questions

4. Identification of Key Themes
- Development of major themes, outcomes of the sub-group discussions

5. Conference/Expert Input
- 2017 IAFP
- International scientific discussions/input
- Information sharing by the European Food Safety Authority (EFSA)

6. Federal Workshop
- Consideration of case studies/practical application
- Derivation of prioritized “next steps”

7. Action Plan
- Utilize prioritized “next steps” from workshop
- Coordination/consultation with Gen-FS

Work Group Discussion Questions

1. What unique information/ knowledge does WGS data provide to this component of QMRA?

2. What risk management questions (i.e., primary decision context) could be addressed by utilizing WGS data in this component of QMRA?

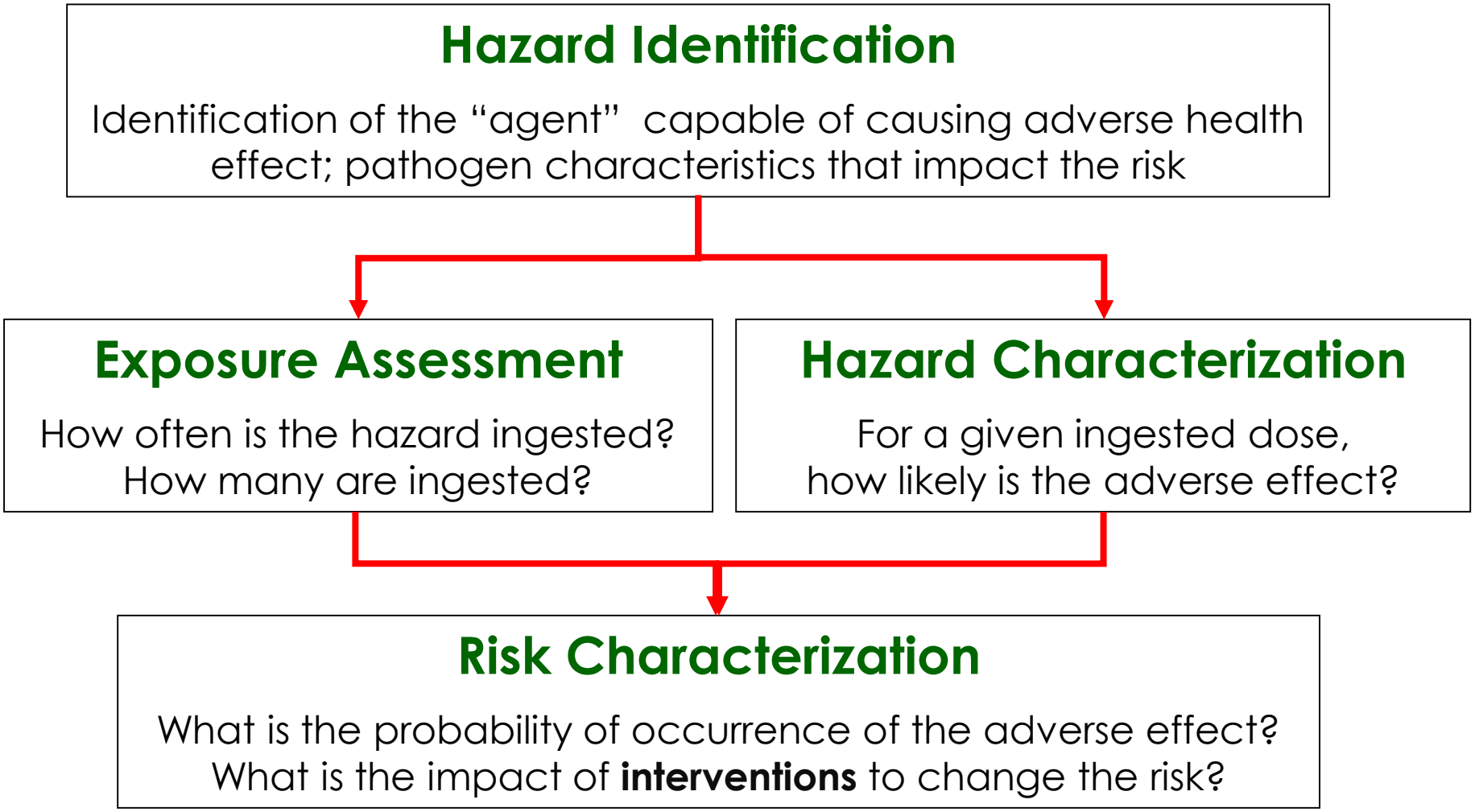
3. What kinds of WGS and related data are needed to enhance its utility for use in risk assessment?

4. What other observations do you have that would benefit from additional discussion/review by the IRAC WGS workgroup?

5. What are the current knowledge gaps in applying WGS information to QMRA and what information is needed?

6. How can WGS information be used to assess risk outside of a QMRA (e.g., risk profile)?

Application of WGS to Risk Assessment



Application of WGS to Risk Assessment Models

How does genomic data from WGS relate to risk?

- Acid Resistance
- Ability to form biofilms
- Oxidation Resistance
- Heat Resistance
- Cold Tolerance

$P(exp)$

- Increased Virulence
- Increased Invasiveness
- Increased Pathogenicity

$P(ill \mid exp)$

- **Antibiotic Resistance**

?

Define "Risk":

- Per serving risk of illness: $P(ill \mid exp)$
- Per annum (number of illnesses)
- More severe outcomes (e.g., hospitalizations)
- Difficult to treat cases of foodborne infection (e.g., AMR)
- Attributable fraction of illnesses to a food

Findings – Themes

- Opportunities
- Challenges
- Data Needs

"Opportunity" Themes

- Refined definition and characterization of "hazard" based on the presence of **specific genes** associated with clinical cases (e.g., virulence)
- Improved "evidence" base for decision-making; enhance certainty of linkage between cases, foods, sources, risk factors
- "Big data;" hazard-based "flags" of concern (predictive analytics/machine learning; e.g., identify associations)
- Near term improvements in **attribution** of cases to a specific foods with recent improvements in outbreak detection and linkage of cases to foods using WGS

"Challenge" Themes

- Expression of genes – translation of genomic information to phenotype
- To date, generating omic data does not support risk assessment, except maybe for hazard identification (Membré & Guillou, Curr Op Food Sci 2016;8:120–126)
- Pathogenicity is multifactorial; survival, completion and colonization, virulence (Risk = Exposure * Hazard)
  - Consideration of completed genomic information profile (virulence, survival, persistence, etc.)
- Need scientific agreement on core virulence genes to define/differentiate foodborne hazards

"Data Needs" Themes

- Markers/genes associated with phenotypes (e.g., virulence)
- Identification of heat resistant or acid resistant variants (survival of subtypes)
- Studies to understand the interrelationship between "dose" versus "virulence" (and AMR)
- Dose-response data (from animal studies) for specific pathogenic strains (defined with certain genomic makers)
- Meta data of sequenced isolates with source information
  - Hazard/food, source, "host" factors, attenuating factors
- Develop more information on associations (e.g., GWAS); need biological verification

Interagency Discussion – Take Away

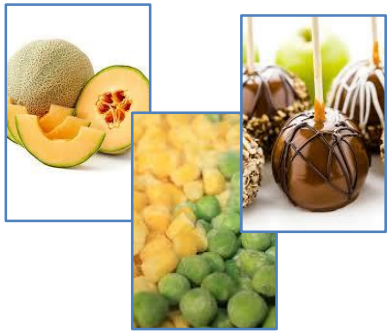
- Differentiate near term vs. long term goals
- Requires on-going cross-disciplinary collaboration and dialogue to include risk assessors
- Near term: WGS support of epidemiological linkage of cases/foods/environment/risk factors; better data for QMRA
- Exploration of **case studies** useful for moving from discussion to application of WGS to QMRA
- Long term: Interlinked “big data” may result in predictive analytics as a reality for assessing potential risks (“flags”)

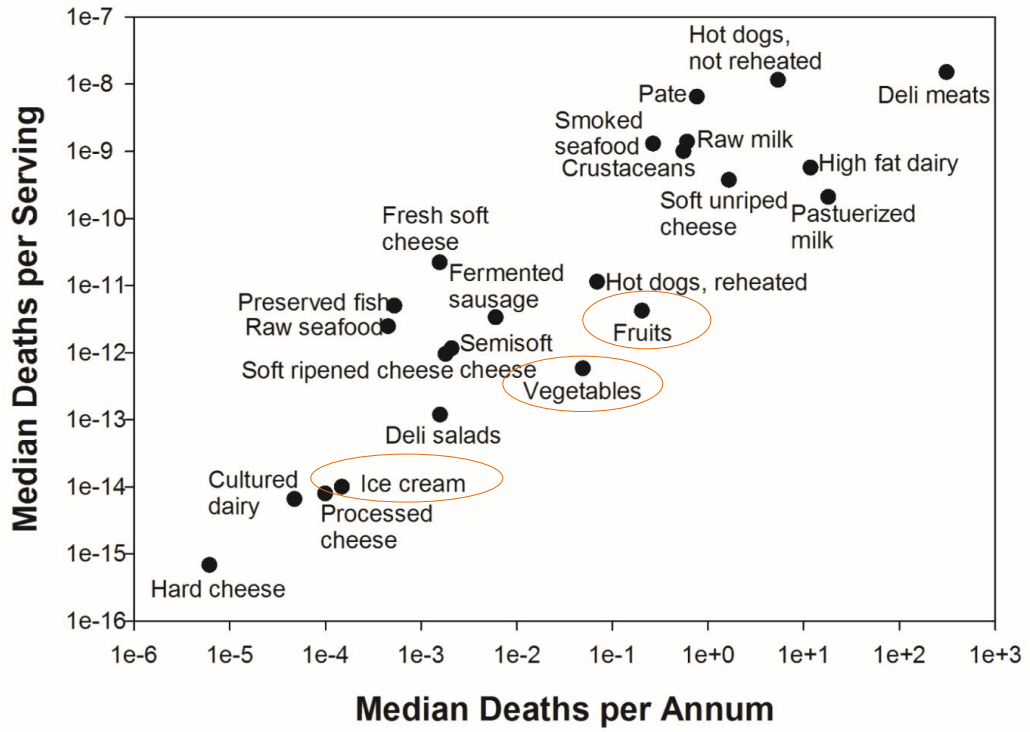
Case Study: *Listeria monocytogenes* (*Lm*) in RTE Foods

- Most outbreaks are linked to ready-to-eat foods that support the growth of *Lm*
- Most listeriosis cases occur among susceptible populations
  - Pregnant women/fetuses
  - Immunocompromised individuals
  - Older adults (> 65 yrs old)
- Most listeriosis cases result from exposure to high levels of *Lm*

Changing Risk…

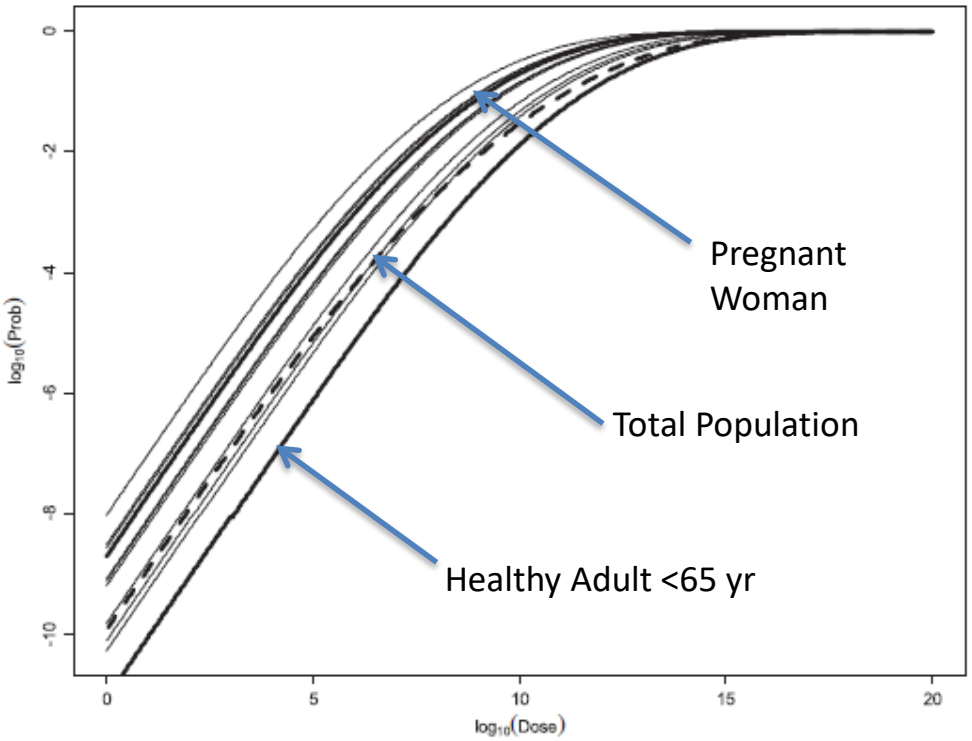
- Outbreaks associated with previous “low” or “moderate” risk foods
- Listeriosis among healthy children
- Listeriosis associated with food not expected to support Lm growth
- Listeriosis at low *Lm* levels

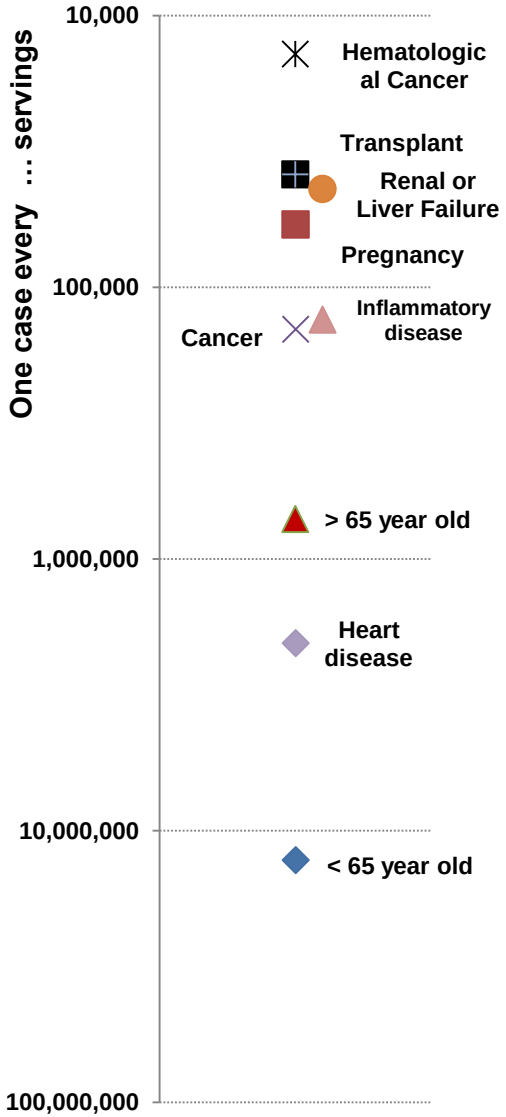




Current outbreaks compared to the findings from the 2003 risk-ranking of ready-to-eat foods.

L*m* Dose-Response





Pouillot, R., Hoelzer, K., Chen, Y., Dennis, S., 2015. Listeria monocytogenes Dose Response Revisited – Incorporating Adjustments for Variability in Strain Virulence and Host Susceptibility. Risk Analysis, 3536, 90-108.

Case Study: *Listeria monocytogenes* (L*m*) in RTE Foods

Potential insights from WGS analysis to understand the changing landscape of L*m* outbreaks

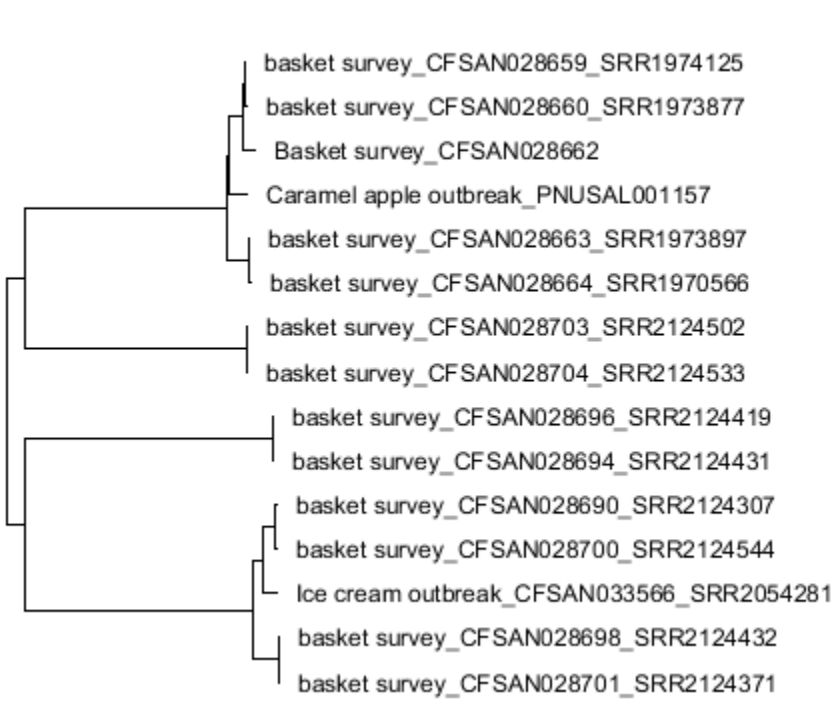
L*m* Market Basket Survey

- 16 ready-to-eat food categories (FDA and FSIS products)
- Sampling design: retail stores in four FoodNet sites across the U. S.
- Total ~27,400 samples collected & analyzed
  - Prevalence and levels
  - Isolates with robust meta data

Luchansky et al, 2017. Journal of Food Protection, 80:903-921.

Collaboration among FDA, USDA /FSIS, USDA/ARS, & Academia

An Example – Retail Market Basket Survey



	ST	CC	LIPI-3, LIPI-4, full length inlA		
basket survey_CFSAN028659_SRR1974125	1	CC1	+	-	+
basket survey_CFSAN028660_SRR1973877	1	CC1	+	-	+
Basket survey_CFSAN028662	1	CC1	+	-	+
Caramel apple outbreak_PNUSAL001157	1	CC1	+	-	+
basket survey_CFSAN028663_SRR1973897	1	CC1	+	-	+
basket survey_CFSAN028664_SRR1970566	1	CC1	+	-	+
basket survey_CFSAN028703_SRR2124502	782	CC2	-	+	+
basket survey_CFSAN028704_SRR2124533	782	CC2	-	+	+
basket survey_CFSAN028696_SRR2124419	296	CC88	-	+	+
basket survey_CFSAN028694_SRR2124431	296	CC88	-	+	+
basket survey_CFSAN028690_SRR2124307	5	CC5	-	-	+
basket survey_CFSAN028700_SRR2124544	5	CC5	-	-	+
Ice cream outbreak_CFSAN033566_SRR2054281	5	CC5	-	-	+
basket survey_CFSAN028698_SRR2124432	5	CC5	-	-	+
basket survey_CFSAN028701_SRR2124371	5	CC5	-	-	+

Acknowledgement:
* Preliminary analysis; Dr. Yi Chen (FDA/CFSAN) and the Interagency LmMBS Team, personal communication

Information obtained from WGS analysis

Identification of clonal groups

Relationship with previous outbreak strains and sporadic clinical strains

Presence of major virulence genes and stop codons

Persistence of strains

Work Group Action Plan

- **Collaboration** – Engage risk assessors as part of the broader dialogue on the application of WGS to food safety
  - Interagency Collaboration on Genomics and Food Safety (Gen-FS)
- **Pilot Project** – FDA, FSIS, and ARS will explore WGS analyses of isolates from the L*m* Market Basket Survey
- **Approach** – Develop comprehensive analytic plans, clarify "risk" to be addressed, and guide specific "omic" data and related meta needs
- **Data Needs/Research:** Identify key data needs and potential funding sources for research in those areas

Thank you.

More information is available at: http://foodrisk.org/irac/home