

Background: Workgroup Initiative & Timeline

Exploration of the Implications of Whole Genome Sequencing on the Conduct and Application of Risk Assessment in Food Safety Decision-Making

September 27, 2017

Project Purpose

Evaluate and the implications of advancements in pathogen subtyping, using whole genome sequencing (WGS), on the conduct and application of food safety risk assessment in federal food safety decision-making. Concomitantly, evaluate the value of using a risk analysis framework to guide the collection of pathogen WGS from food, environment, and clinical samples along with metadata to inform various types of food safety risk management decisions.

Background

In December 2016, the Interagency Risk Assessment Consortium (IRAC) accepted an interagency proposal to explore the implications and application of whole genome sequencing in assessing food safety risks in federal decision-making.

Federal agencies increasingly rely on risk assessment using a variety of analytic tools to guide food safety decisions from production to consumption, such as on-farm controls to mitigate the spread of microbiological hazards and guidelines to effectively mitigate food safety risks. One scientifically-based analytic tool that has received broad acceptance nationally and internationally is quantitative microbiological risk assessment (QMRA). QMRA is well recognized as an objective, transparent, and structured approach for quantitatively evaluating risk management alternatives for mitigating food safety risks. QMRAs consist of four primary steps (FAO/WHO, 1999¹):

- **Hazard Identification** – *The identification of the biological agent(s) capable of causing adverse health effects and which may be present in a particular food or group of foods.*
- **Exposure Assessment** – *The evaluation of the likely intake of a biological agent(s) via food as well as exposures from other sources if relevant.*
- **Hazard Characterization (Dose-Response)** – *The evaluation of the nature of the adverse health effects associated with biological agent(s) which may be present in food.*

¹ Codex Alimentarius Commission. 1999. Principles and Guidelines for the Conduct of Microbiological Risk Assessment. CAC/GL-30.

- **Risk Characterization** – An estimation, including attendant uncertainties, of the probability of occurrence and severity of known or potential adverse health effects in a given population based on hazard identification, hazard characterization and exposure assessment

While the primary steps in a QMRA remain the same, the conduct and application of QMRAs as food safety decision-support tools has evolved over the past 20 years. QMRAs have been increasingly tailored to inform specific risk management decisions (Dennis et al., 2008, Dearfield et al., 2014²). As such, these QMRA frameworks have been used to inform the collection of targeted data to fill information gaps and enhance the usefulness of these predictive tools (Chen and Schaffner 2013).³ However, just as QMRAs inform decisions on what data to collect or research to conduct, rapid advancement in science and information technology can change how QMRAs are conducted and the types of decisions they can inform.

With the rapid evolution in pathogen subtyping and broad acceptance and use of omics technologies such as whole-genome sequencing (WGS) for foodborne outbreak detection and source tracking, the Interagency Risk Assessment Consortium and others in the food safety risk assessment community anticipate^{4,5,6} that this newer technology may also influence how food safety risks are assessed and managed, including the conduct and application of food safety QMRAs. Currently, there is limited exploration of the impact of WGS on the conduct and application of food safety risk assessment or how QMRA may provide a structure for guiding the collection of WGS data and related metadata to inform a broader array of well-defined risk management decisions.

WGS provides maximum resolution for DNA-based characterization of pathogens. While data interpretation remains a challenge (e.g., translation into physiological behavior), the rapidly decreasing costs, timely generation of more robust and discriminate subtyping information has led to increased use of WGS in foodborne disease surveillance and use in federal testing of foods and the environment. As these advancements in subtyping revolutionize outbreak surveillance, pathogen source tracking, and characterization of these hazards, including

² SB Dennis, Kause J, Losikoff M, Engeljohn DL, and Buchanan RL. 2008. Using risk analysis for microbial food safety regulatory decision-making, pp. 137-176. In D.W. Schaffner (ed.), *Microbial Risk Analysis of Foods*. ASM Press, Washington, DC; KL Dearfield, Hoelzer K, and Kause JR. 2014. Review of various approaches for assessing public health risks in regulatory decision making: choosing the risk approach for the problem. *J Food Prot* 77(8): 1428-40 [2011-2013 IRAC Working Group deliverable: http://foodrisk.org/default/assets/File/IRAC_Work_Group_Clarification_of_the_Various_Approaches_for_Assessing_Risk_2011-2013.pdf (accessed November 28, 2016)].

³ IRAC co-sponsored 2013 International Association for Food Protection symposia: *Making a Difference: Data Collection for Risk Assessments through Innovative Approaches* [available at: <https://iafp.confex.com/iafp/2012/webprogram/Session1180.html> (accessed March 2, 2017)]

⁴ S. Brul, Bassett J, Cook P et al. 2012. ‘Omics’ technologies in quantitative microbial risk assessment. *Trends in Food Science & Technology* 27: 12-24.

⁵ International Association for Food Protection European Symposium. Workshop: Next Generation MRA (Microbial Risk Assessment) – Integration of Omics Data into Assessment. Co-organizers: International Life Science Institute Europe, International Association for Food Protection, and the International Commission on Microbiological Specifications for Foods. 13-14 May, 2016. Athens, Greece. See: http://ilsi.org/wp-content/uploads/2016/08/ILSI-WS-Next-Generation-MRA_Prof.-Banati.pdf

⁶ International Association for Food Protection European Symposium on Food Safety. How to Exploit Omics Data on Pathogen Behavior in Microbiological Risk Assessment: An Update on the Current Research. March 29, 2017. Brussels, Belgium. See: <https://iafp.confex.com/iafp/euro17/webprogram/Session3629.html>

tracking drug resistance across the farm-to-table continuum, we wonder how best to leverage this tool to support decision-making. Specifically, we want to know:

- *What are the primary food safety decision contexts (e.g., recalls, major policies, etc.)?*
- *How will this new science impact the various components of QMRA (hazard identification, hazard characterization, exposure assessment, and risk characterization)?*
- *Will changes be limited to the traditional components of food safety QMRAs or will these new data more broadly transform both the conduct and application of QMRAs?*
- *What are the opportunities and challenges in using WGS information in QMRAs?*
- *Can QMRA provide structure to collecting and interpreting WGS data (including meta data during traceback investigations) to further their utility in regulatory decision-making?*

Table 1. Working Group Members

Agency	Member
USDA, Food Safety and Inspection Service	Karen Becker, Philip Bronstein, Evelyn Mbandi, Uday Dessai, Emilio Esteban, Janell Kause,* Kis Robertson Hale, Gurinder Saini
FDA, Center for Food Safety and Applied Nutrition	Marc Allard, Eric Brown, Sherri Dennis*, Sofia Santillana Farakos
CDC, National Center for Emerging and Zoonotic Infectious Diseases	Arthur Liang
CDC, National Institute for Occupational Safety and Health	Brett Green
FDA, Office of Foods and Veterinary Medicine	Barry Hooberman
NIH, National Institute of Allergy and Infectious Diseases	Robert Hall
USDA, Agricultural Research Service	Andy Hwang
USDA, Animal and Plant Health Inspection Service	Wendy Hall, Randall Levings, Tod Stuber
USDA, National Institute for Food and Agriculture	Max Teplitski
USDA, Office of the Chief Scientist	Sheila Fleischhaker

*Co-leads: Janell Kause (U.S. Department of Agriculture, Food Safety and Inspection Service) and Sherri Dennis (Food and Drug Administration, Center for Food Safety and Applied Nutrition)

Working Group members and staff volunteered to explore the implications of WGS on key components of conducting food safety risk assessment (e.g., hazard identification, exposure assessment, hazard characterization/dose-response, and/or risk characterization; Table 2). Twelve interagency meetings were held in FY2017, February – June 2017.

Table 2. Risk Assessment Subgroups*

Sub-Groups	Member
Hazard Identification <ul style="list-style-type: none"> Mar. 22nd meeting -- responses to specific questions, 1-3 (p. 5) Apr. 19th meeting – responses to specific questions, 4-5 (p. 5) Jun. 22nd meeting – primary themes to all 6 questions (p.5) 	Michael Bazaco, FDA Stephanie Defibaugh-Chavez, FSIS Uday Dessai, FSIS Emilio Esteban, FSIS Brett Green, CDC Wendy Hall, APHIS Randall Levings, APHIS Arthur Liang, CDC Tamika Payne, FSIS Aurelie Pohl, FDA Tod Stuber, APHIS Max Teplitski, NIFA Jie Zheng, FDA
Exposure Assessment <ul style="list-style-type: none"> Apr. 3rd meeting -- responses to specific questions, 1-3 (p. 5) Apr. 26th meeting – responses to specific questions, 4-5 (p. 5) Jun. 28th meeting – primary themes to all 6 questions (p.5) 	Karen Becker, FSIS Yi Chen, FDA Eric Ebel, FSIS Kathy Gensheimer, FDA Brett Green, CDC Andy, Hwang, ARS Sofia Santillana Farakos, FDA Kis Robertson Hale, FSIS Mike Williams, FSIS
Hazard Characterization <ul style="list-style-type: none"> Apr. 6th meeting -- responses to specific questions, 1-3 (p. 5) Apr. 27th meeting – responses to specific questions, 4-5 (p. 5) Jun. 27th meeting – primary themes to all 6 questions (p.5) 	Karen Becker, FSIS Uday Dessai, FSIS Eric Ebel, FSIS Sheila Fleischhaker, OCS Robert Hall, NIH Andy Hwang, ARS Julie Kase, FDA Randall Levings, APHIS André Markon, FDA Kis Robertson Hale, FSIS Sofia Santillana Farakos, FDA Mike Williams, FSIS
Risk Characterization <ul style="list-style-type: none"> Apr. 7th meeting -- responses to specific questions, 1-3 (p. 5) Apr. 24th meeting – responses to specific questions, 4-5 (p. 5) Jun. 13th meeting – primary themes to all 6 questions (p.5) 	Marc Allard, FDA Eric Ebel, FSIS Barry Hooberman, FDA Cary Parker, FDA

- Sherri Dennis (FDA) and Janell Kause (FSIS) will be actively involved in all sub-groups.

Key Questions

Specific questions addressed by the subgroup members:

- i. What unique information/ knowledge does WGS data provide to this component of QMRA?
- ii. What risk management questions (i.e., primary decision context) could be addressed by utilizing WGS data in this component of QMRA?
- iii. What kinds of WGS and related data are needed to enhance its utility for use in risk assessment?
- iv. What other observations do you have that would benefit from additional discussion/review by the IRAC WGS workgroup?
- v. What are the current knowledge gaps in applying WGS information to QMRA and what information is needed?
- vi. How can WGS information be used to assess risk outside of a QMRA (e.g., risk profile)?

Scientific Literature

*Relevant peer reviewed scientific publications available on Interagency Risk Assessment Consortium website:
<http://foodrisk.org/workgroup-members>

2017 Webinars*

<p>Date: March 16, 2017, 12:30-2 pm ET (facilitator: Randy Duverna, FSIS/Science Staff)</p> <p>Presenter: Dr. Eric Brown, Director, Division of Microbiology Office of Regulatory Science, Center for Food Safety and Applied Nutrition, US Food and Drug Administration</p> <p>Presentation: <i>WGS 101: The Rationale, Mechanics, and Impact of WGS for Food Safety</i></p> <p>Location: USDA/FSIS, Room 9-199, Patriot Plaza III, 355 E. Street SW, Washington, DC; Webinar</p>
<p>Date: April 13, 2017, 1-2:30 pm ET</p> <p>Presenter: Dr. Ian Williams, Chief, Outbreak Response and Prevention Branch, Division of Foodborne, Waterborne, & Environmental Division, National Center for Emerging and Zoonotic Infectious Diseases, Center for Disease Control and Prevention Office of Regulatory Science, Center for Food Safety and Applied</p> <p>Presentation: <i>Whole Genome Sequencing: The Transformation of Surveillance and Outbreak Investigation for Foodborne and Enteric Pathogens</i></p> <p>Location: Webinar (facilitator: Jude Smedra, FSIS/Science Staff)</p>
<p>Date: May 24, 2017, 3-4 pm EDT</p> <p>Presenter: Martin Wiedmann, Gellert Family Professor in Food Safety, Department of Food Science,</p>

<p>Cornell University Presentation: <i>hqSNP, wgMLST and the WGS alphabet soup: what epidemiologists need to know</i> Location: Webinar hosted by Cornell University; slide set and recordings can be found at: https://nyfoodsafety.cals.cornell.edu/molecular-epidemiology/webinars</p>	<p>Date: October 11, 2017, 1-2:30 pm ET Presenter: Dr. Arie Havelaar, Professor, Microbial Risk Assessment and Epidemiology of Foodborne Diseases, Emerging Pathogens Institute, University of Florida; Dr. Trudy Wassenaar, Director, Molecular Microbiology and Genomics Consultants, Zotzenheim, Germany Presentation: <i>Whole Genome Sequencing – Application in Quantitative Microbial Risk Assessment</i> Location: Webinar (facilitator: Jude Smedra, FSIS/Science Staff)</p>
<p>Date: October 18, 2017, 1-2:30 pm ET Presenter: Dr. Francisco Zagmutt, EpiX Analytics; Dr. Paul Morley, Professor, Colorado State University, Ft. Collins, Colorado Presentation: <i>Assessing Antimicrobial Resistance Risks in Food: Can We Do Better Using Whole Genome Sequencing?</i> Location: Webinar (facilitator: Jude Smedra, FSIS/Science Staff)</p>	

*Recorded presentation on Interagency Risk Assessment Consortium website: <http://foodrisk.org/workgroup-members>

**Presentations in the New York Integrated Series for the Centers for Excellence are found at this link: <https://nyfoodsafety.cals.cornell.edu/molecular-epidemiology/webinars>

2017 Workshop

The Interagency Risk Assessment Consortium (IRAC) is hosting a federal workshop on September 27, 2017 to explore the practical application of whole genome sequencing (WGS) data to advance how federal agencies assess microbiological food safety risks for purposes of guiding risk management decisions. It is the culmination of multi-disciplinary, cross-agency discussions on how WGS may provide improved data, including enhanced epidemiological linkage of clinical cases of illness to food source, insights to new intervention options to reduce contamination and prevent foodborne illnesses, and an enhanced understanding of consumer exposure to specific strains of a foodborne pathogen that result in illness. Specifically, the workshop explores case studies on assessing risks associated with *Listeria monocytogenes* in ready-to-eat foods and *Salmonella* in poultry, considering the following:

- *Primary food safety decision contexts (e.g., recalls, major policies, etc.);*
- *How this new data might lead to changes or inform traditional components of food safety risk assessments and/or transform the approaches used to assess food safety risks altogether;*
- *Opportunities and challenges in applying WGS information to food safety risk assessment; and*
- *Utility of the risk analysis framework to guide the collection and interpretation of WGS and related meta data*

The expected outcome of the workshop will be a ranking of options for “next steps” used in the development of an interagency action plan to for the application of WGS to advance food safety risk assessment.

Work Group Deliverables

Working group activities and deliverables:

- Identify **types of risk management decisions and related questions** for the application of WGS in evaluating food safety risks.
- **Review scientific literature** on WGS and assessing food safety risk and role in decision-making. IRAC Working Group password protected website on Foodrisk.org.
- **Hold webinars and symposia** among federal partners and invited national and international scientists to derive a shared understanding of the emerging field of WGS and its current application in epidemiology and potential application to improve risk assessment and decision-making.
- **Host a scientific workshop** among federal scientists to discuss how risk assessment can guide WGS research and how WGS can further improve food safety risk assessment. IRAC members and invited experts will also explore the broader application of WGS in food safety decision-making.
- **Develop an action plan** representing current U.S. federal thinking on the next steps in applying WGS to assess food safety risks, use of the risk analysis framework to identify data needs, and corresponding implications on food safety decision-making.

Timeline



