



United States Department of Agriculture

One Team, One Purpose



Food Safety and Inspection Service

Protecting Public Health and Preventing Foodborne Illness



Food Safety and Inspection Service

Whole Genome Sequencing (WGS) at FSIS: Current Status

Uday Dessai MPH, MS, PhD

Senior Public Health Advisor

Office of Public Health Science, FSIS, USDA

and

FSIS WGS and NARMS Team

Success = One-Team-One-Purpose

Food Safety and Inspection Service

WGS at FSIS: Presentation Outline

- ❑ FSIS Mission and Application of WGS
- ❑ FSIS Success and Current Challenges
- ❑ Focus on Application of WGS
 - ❑ Outbreak Investigations
 - ❑ Antimicrobial Resistance (AMR)
- ❑ WGS Current and Future Focus
- ❑ Healthy People 2020/2030
- ❑ Concluding Remarks

Food Safety and Inspection Service:

WGS at FSIS: Strategic Plans and Application of Scientific Approaches

3 STRATEGIC GOALS

Goal 1: Prevent Foodborne Illness and Protect Public Health

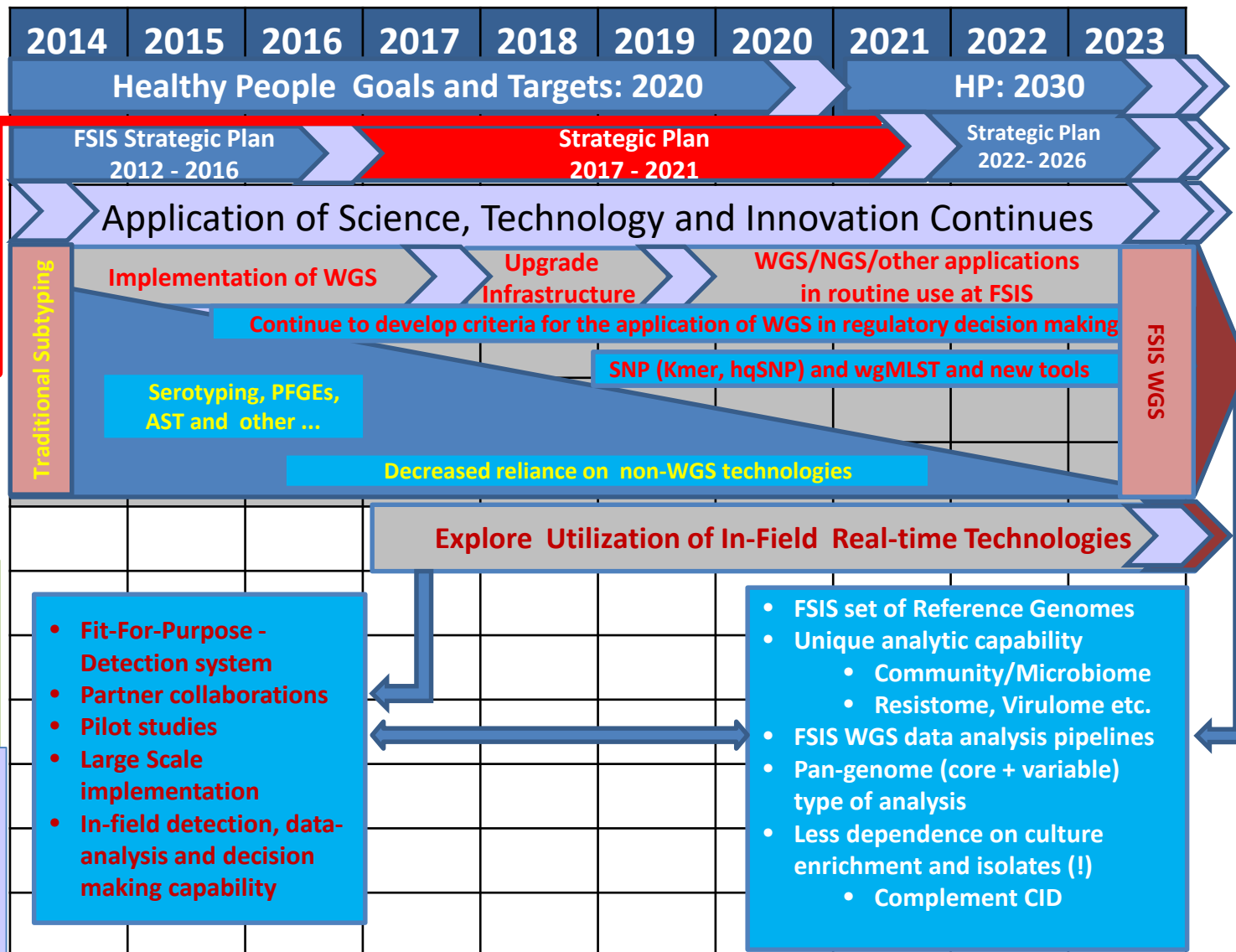


Goal 2: Modernize Inspection Systems, Policies, and the Use of Scientific Approaches



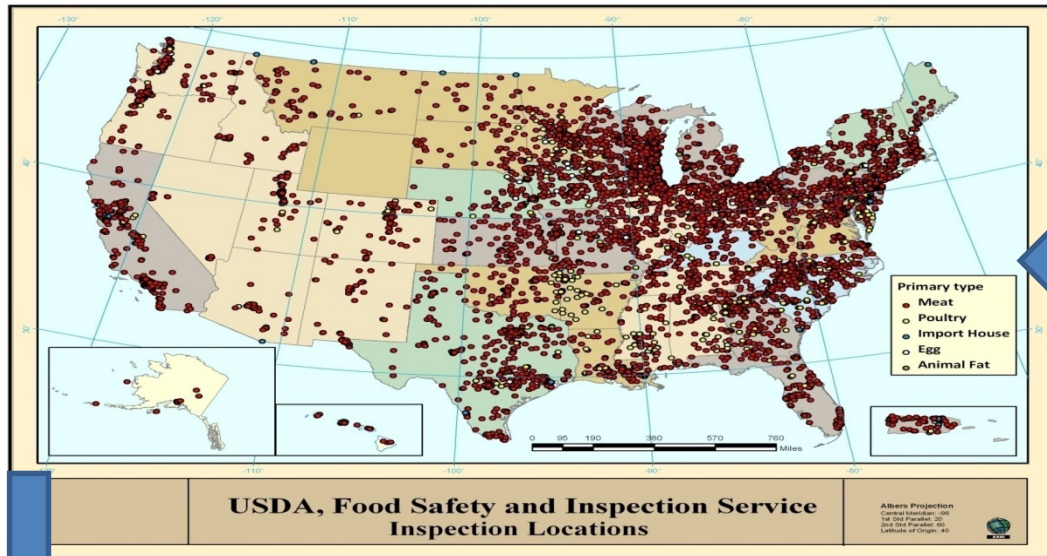
Goal 3: Achieve Operational Excellence

Note:
Strategic Plan 2012-2016
Goal 5 - Effectively Use Science to Understand Foodborne Illness and Emerging Trends



Food Safety and Inspection Service

WGS at FSIS: Our Authority and What We Do!



FSIS is the public health agency in the U.S. Department of Agriculture responsible for ensuring that the nation's commercial supply of meat, poultry, and egg products is safe, wholesome, and correctly labeled and packaged.

Our Authority

- ❑ Federal Meat Inspection Act (FMIA), 1906
- ❑ Agricultural Marketing Act (AMA), 1946
- ❑ Poultry Products Inspection Act (PPIA), 1957
- ❑ Humane Methods of Slaughter Act (HMSA), 1958
- ❑ Egg Products Inspection Act (EPIA), 1970

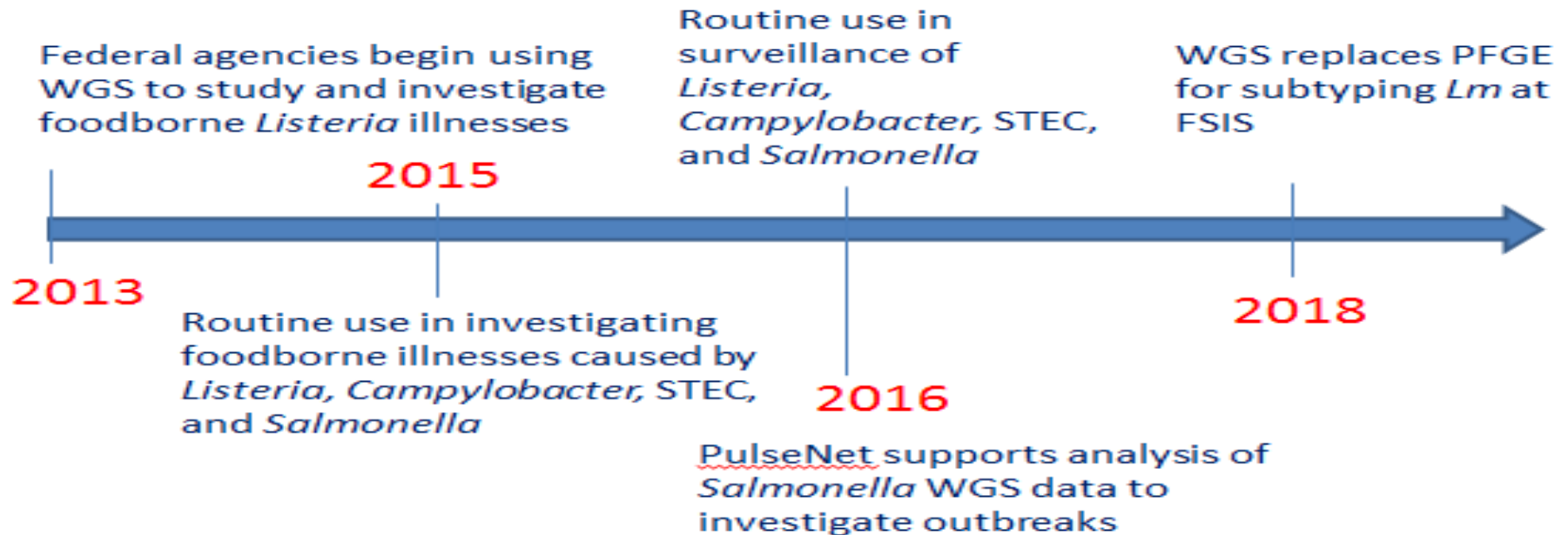
Inspection and Sampling

- ❑ About 6479+ Establishments
- ❑ Over 7970 Inspection Personnel
-
- ❑ > 100 K Microbiological Samples
- ❑ > 256,333 Micro Analyses
- ❑ About 10,000 bacterial isolates
-
- ❑ 3+ million Scientific Analysis (includes residue samples)

Enrichment
Screening
Isolation
Characterization

Food Safety and Inspection Service

WGS at FSIS: Major Milestones



WGS in FSIS Lab System

- ❑ July 2014: *Salmonella* and *Listeria monocytogenes*
- ❑ December 2014: STECs
- ❑ February 2015: *Campylobacter*
- ❑ May 2015: Capability to directly upload WGS files to NCBI

Food Safety and Inspection Service

WGS at FSIS: Potential Applications

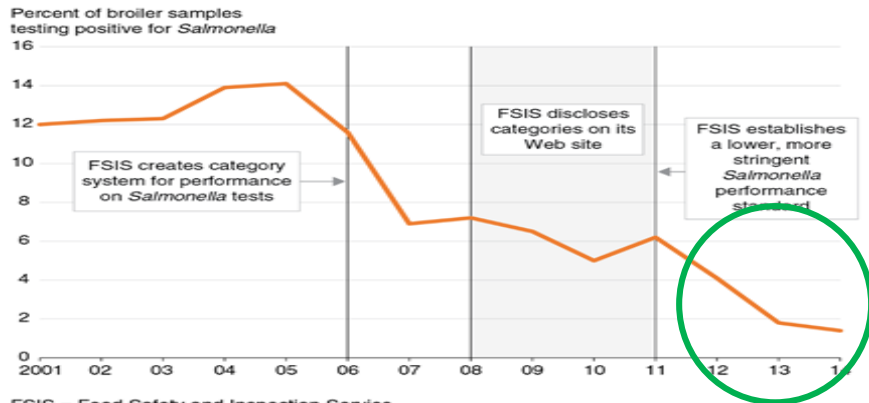
Primary Interest: How can we prevent, control and reduce pathogens of concern in FSIS regulated products

- ☐ Outbreak Investigations
 - ☐ Harborage
 - ☐ Geographic Distribution of Genotypes
 - ☐ Occurrence, Trend and Patterns of Genotypes of Public Health Concern in Regulated Products
 - ☐ Interspecies Movement of Genotypes
-

- ☐ Antimicrobial Resistance (AMR) Genes
- ☐ Biocide Resistance
- ☐ Mobilome
- ☐ Virulence and Pathogenicity Genes
- ☐ Survival and Adaptation Genes

Food Safety and Inspection Service: WGS at FSIS: Pathogen Reduction Success and Challenges

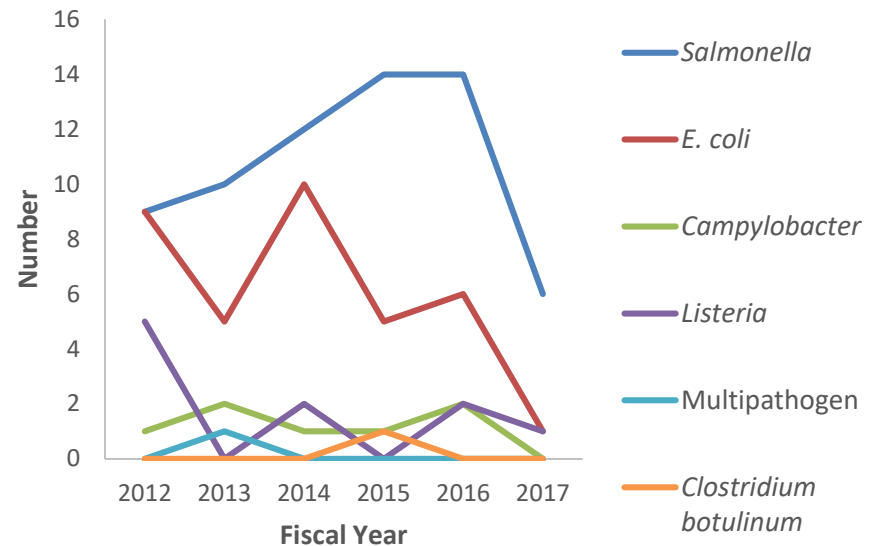
Seventy-five percent of the drop in the percent of broiler samples testing positive for *Salmonella* between 2005 and 2014 correlated with regulatory actions



Success - The decline in *Salmonella* levels enabled FSIS to promulgate a more stringent performance standard for *Salmonella*. In 2011, FSIS lowered the standard for *Salmonella* in broilers from 21.5 percent of samples that tested positive to 9.8 percent.

Source - ERS: <https://www.ers.usda.gov/amber-waves/2017/may/regulation-market-signals-and-the-provision-of-food-safety-in-meat-and-poultry/>

FY 2012-2017 Foodborne Outbreak Investigations by Pathogen (N=120)



- ❑ FSIS regulated products contribute to ~ 310,000 Salmonellosis annually
- ❑ Our collaborative success to reduce *Salmonella* on chicken carcass took almost a decade
- ❑ We are seeing an increase in *Salmonella* investigations and *Salmonella* attribution
- ❑ How can the application of WGS to Food Safety and Public Health help us replicate our success *Salmonella* on chicken carcasses!

Food Safety and Inspection Service:

WGS at FSIS: WGS in Outbreak Investigations

In FY18, we have been engaged in 9 investigations and watches

WGS was helpful in 4 outbreaks

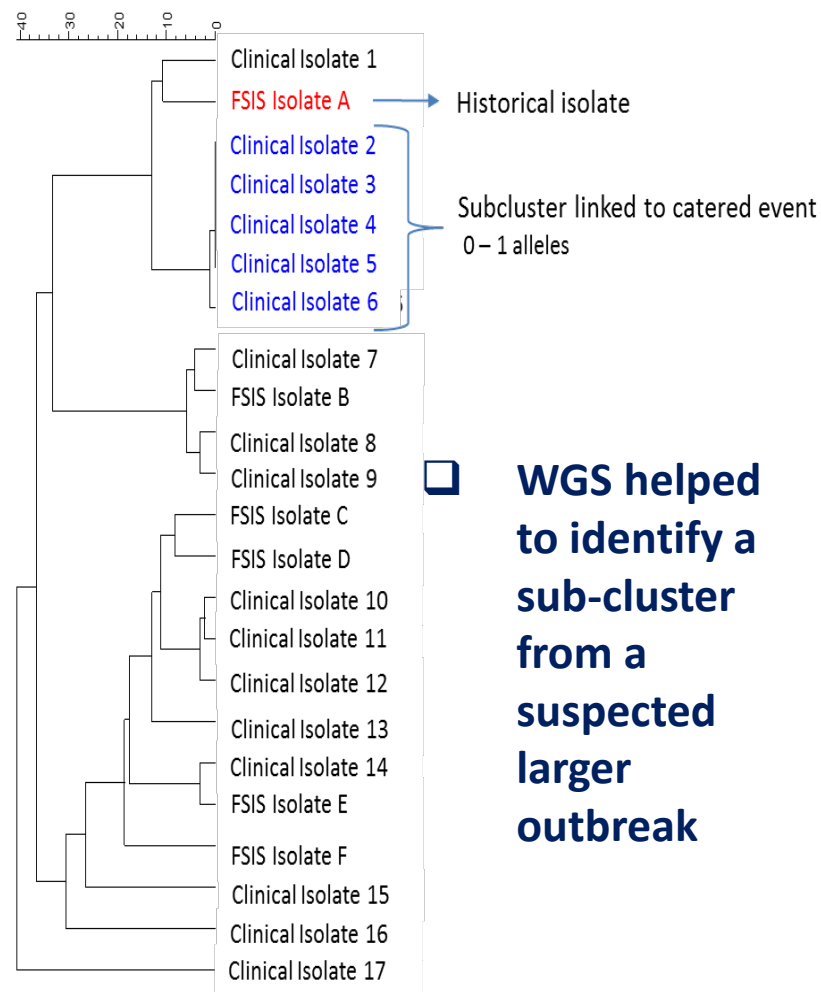
- **The California Marines *E. coli* Outbreak:** WGS helped to identify civilian cases that were closely related to Marines cases
 - This lead helped FSIS to conduct additional traceback to identify the potential source of illnesses
 - A definitive source of illnesses was not identified
- **The Iowa *Salmonella* Typhimurium Chicken Salad Outbreak:** WGS helped rule out cases that were not part of this outbreak
 - CDC final web posting for IA *Salmonella* Typhimurium chicken salad investigation:
<https://www.cdc.gov/salmonella/typhimurium-02-18/index.html>
- **Outbreak-X:** This investigation is ongoing and WGS shows close relatedness in isolates involved and further investigation is looking into slaughter date and source farms etc. WGS helped rule out the connection between this and a similar previous Outbreak
- **Outbreak-Y:** WGS helped connect the FSIS isolates from one of the retail supplier to case-patient isolates
 - The location where case patients purchased the implicated products, did not maintain records/logs, hence despite the use of WGS, traceback could not definitively identify source material used in producing the implicated product. This information was used as the basis to conduct risk evaluation (PHRE) at this establishment.

In addition to WGS Match, epidemiological and source information is essential to connect the patient and the food source(s)

Food Safety and Inspection Service:

WGS Case Study-1: Chicken-Associated *Salmonella* Enteritidis Investigation - 2017

- ❑ July 2017 - CDC notified FSIS about a SE illness cluster with 53 illnesses in 25 states with a PFGE pattern
- ❑ Is this a single outbreak?
- ❑ Although the PFGE pattern was same, further investigation indicated a single sub-cluster in a single state that may not be connected to other illnesses
- ❑ Chicken was traced to a federal establishment and a historic isolate from establishment matched clinical PFGE pattern
- ❑ WGS analysis :
 - ❑ Clinical isolates in sub-cluster are related to each other by 0 SNP differences (0-1 alleles)
 - ❑ Isolates from the sub-cluster were not closely related to the historic product isolate (10-17 SNP differences)
 - ❑ Other clinical isolates not related to sub-cluster isolates

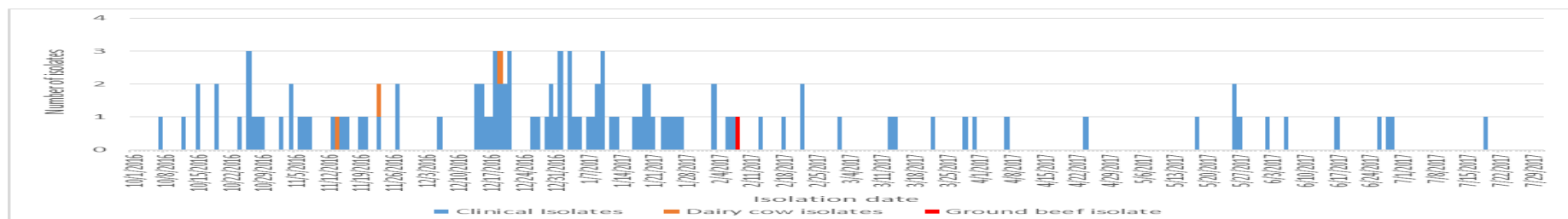


Annotated WGS Tree (Source: CDC)

Food Safety and Inspection Service:

WGS Case Study-2: Beef Associated *Salmonella* Newport - 2017

October 1, 2016–July 31, 2017: Epidemic curve of people infected with *Salmonella* Newport (n=106), isolates from dairy cattle (n=3*), and leftover ground beef (n=1),

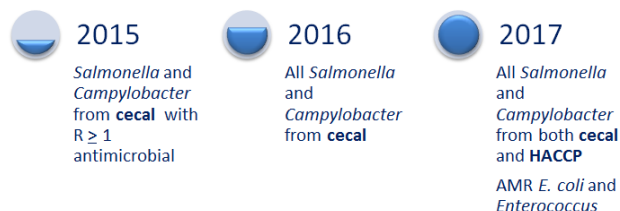


- ❑ Common PFGE pattern, cases in 21 states, majority in Southwest United States
- ❑ 52/65 (80%) reported eating ground beef at home
 - ❑ FSIS traceback identified three slaughter/processing establishments
 - ❑ Outbreak strain isolated from 4 New Mexico dairy cattle
- ❑ Common PFGE pattern – difficult to distinguish sporadic and outbreak cases
- ❑ hqSNP analysis showed that all 106 isolates were closely related (0–12 SNPs)
- ❑ WGS analysis provided more discriminatory power to refine the outbreak case definition to one specific genetic clade
- ❑ The separate clade within the PFGE pattern had distinct epidemiology and was investigated separately

Food Safety and Inspection Service

WGS at FSIS: NARMS - Application of WGS and Detection of Novel Genes

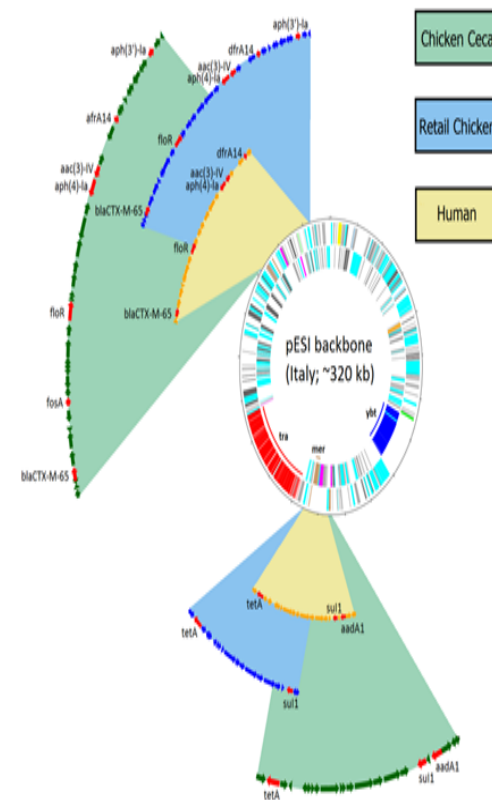
Genotypic screening for antimicrobial resistance using whole genome sequencing (WGS)



- Ability to rapidly identify new genes of concern
 - Work with NARMS and other partners in a real-time to identify the presence, magnitude and impact of undesirable gene(s)
 - Proactively work with stakeholders to start taking the necessary actions
- Examples of WGS application to novel gene detection and actions
 - ESBL *bla*_{CTX-M-65}
 - Colistin Resistance
 - Quinolone Resistance
 - Linezolid Resistance
 - Daptomycin Resistance

□ The *bla*_{CTX-m_65} gene is located in a multiresistance region and confers resistance to 5 other antimicrobial classes:

- Florfenicol/Chloramphenicol
- Sulfisoxazole, Trimethoprim/Sulfamethoxazole
- Tetracycline
- Fosfomycin
- Aminoglycosides



An FDA-CDC-FSIS Paper: [Antimicrob Agents Chemother](#). 2017 Jun 27;61(7). pii: e00488-17. doi: 10.1128/AAC.00488-17. Print 2017 Jul Press
Title: Comparative Analysis of Extended-Spectrum-β-Lactamase CTX-M-65-Producing *Salmonella enterica* Serovar *Infantis* Isolates from Humans, Food Animals, and Retail Chickens in the United States

Food Safety and Inspection Service

Salmonella Infantis and *bla*CTX-M-65 Distribution Over Time

- ❑ Distribution of the *bla*CTX-M-65 gene among PFGE types of *Salmonella* Infantis Isolates from FSIS (2015 -2017)
 - ❑ In 2015 distribution was limited to one PFGE type and the number of isolates carrying this gene were only six
 - ❑ In 2016 distribution increased to seven PFGE types and the total isolates carrying this gene increased to 51
 - ❑ In 2017 distribution increased to 22 PFGE types and the total isolates carrying this gene increased to 140
- ❑ Distribution of the *bla*CTX-M-65 gene among PFGE types of *Salmonella* Infantis Isolates from NCBI (Feb-2018)
 - ❑ 34.75% FSIS isolates designated as Infantis on NCBI carry *bla*CTX-M-65 (384/1105)
 - ❑ There are 19 NCBI SNP Clusters for Serovar Infantis
 - ❑ Cluster PDS000003955.213: Contains 304 Clinical and 399 FSIS isolates that carry *bla*CTX-M-65
 - ❑ Upload by Year:

Year	2015	2016	2017	2018 (to date)
NCBI Uploads	19	64	195	107

Food Safety and Inspection Service:

WGS at FSIS: Where Do We Go From Here

WGS: Future

Communication and Training

- ❑ Need to standardize and simplify WGS related communications
- ❑ Availability of audience specific WGS training modules
- ❑ Continued engagement (Meetings, Webinars, FAQs etc.)

Data Sharing, Tools and Interpretation

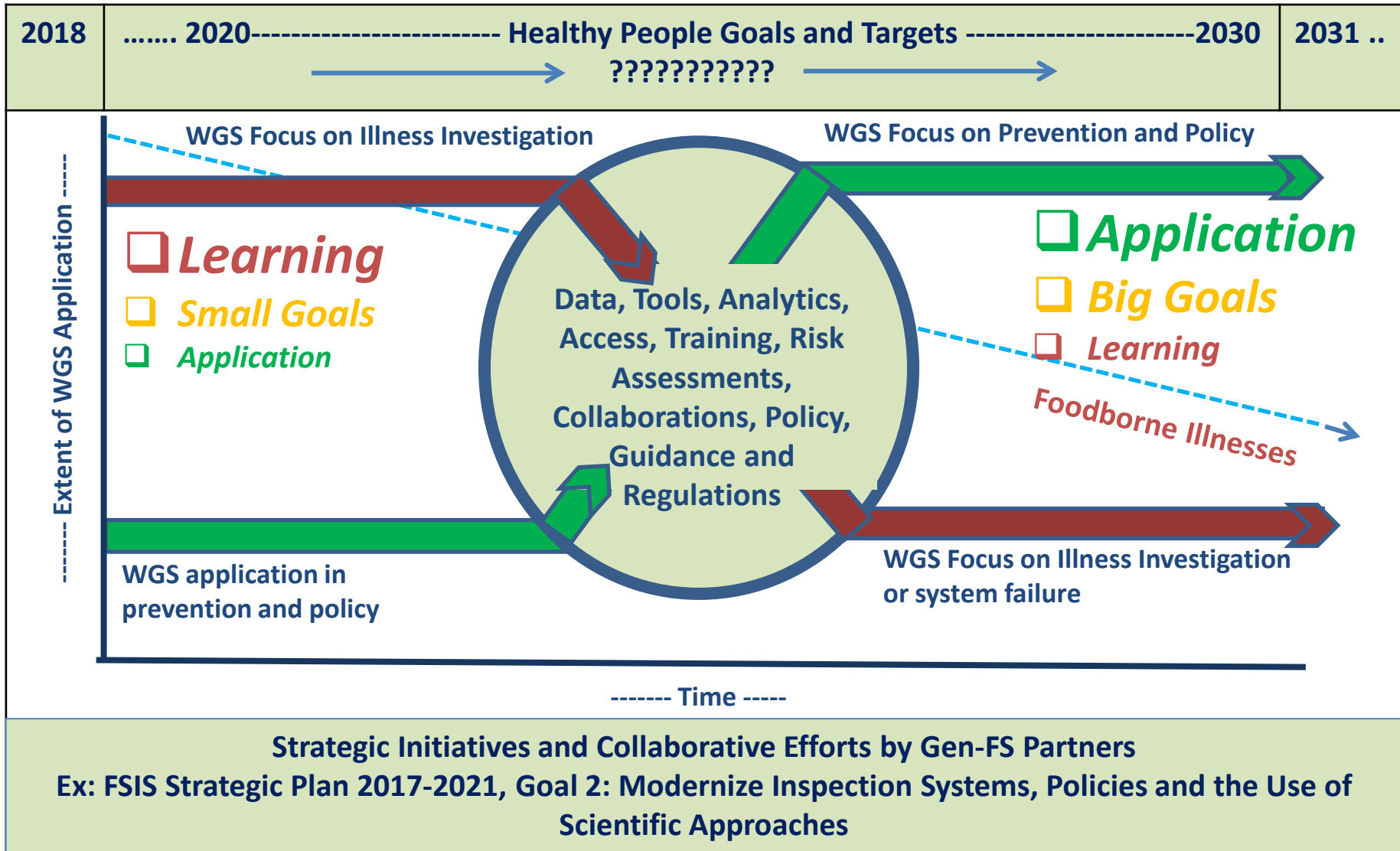
- ❑ Development of WGS public databases that are robust
 - ❑ Need to capture WGS diversity
 - ❑ Data sharing opportunities
- ❑ Readily accessible and user friendly analysis and interpretation tools
- ❑ Opportunity for establishing Public-Private Partnership(s)

Illness Prevention Focus and Collaborations

- ❑ WGS in Risk and Attribution
 - ❑ Phenotype to Genotype focus
 - ❑ Virulence, Pathogenicity, Adaption, Gene mobility
- ❑ Transience vs Harborage and Safe-Harbor Issue
- ❑ Use in routine inspection process
- ❑ Pathogen introduction and movement among animal, humans, environment and establishments/factories
- ❑ Discussion and clarity on legal issues and ramifications
- ❑ Opportunities for collaborations and data sharing
- ❑ Healthy People 2030 Goals

Food Safety and Inspection Service:

WGS at FSIS: Where Do We Go From Here: Healthy People 2030



Food Safety and Inspection Service

FSIS WGS Update: WGS - A Collaborative Undertaking


☐ FSIS - WGS Collaborations



U.S. Department of Health and Human Services



Illinois Institute of Technology




FDA

**U.S. FOOD & DRUG
ADMINISTRATION**




Innovation Through Collaboration
IFSH INSTITUTE FOR
FOOD SAFETY
AND HEALTH



CDC

Centers for Disease Control and Prevention
CDC 24/7: Saving Lives, Protecting People™



USDA

United States Department of Agriculture
Food Safety and Inspection Service



NCBI

National Center for
Biotechnology Information


FSIS is actively engaged in partnerships/collaborations

- ☐ **Gen-FS: An Interagency Collaboration on Genomics and Food Safety**
- ☐ **IFSH: A FDA-Industry-IIT collaboration**
- ☐ **GMI: Global Microbial Identifier – Mission is to establish a global and connected genomic database/system**
- ☐ **WHO – WHO/PAHO guidance on WGS for developing countries**
- ☐ **IRAC – Use of WGS in QMRA**



USDA

ARS and APHIS



**World Health
Organization**

Global Microbial Identifier



GMI

Global Microbial Identifier

Food Safety and Inspection Service:

WGS at FSIS: Summary Points

- ❑ Based on our Strategic Plan and Healthy People Goals (2020/2030) our pathogen reduction goals and our challenges are well defined
- ❑ FSIS has build sufficient capacity for conducting WGS on all FSIS pathogen isolates
 - ❑ In FY 2017 FSIS sequenced over 7200 isolates
 - ❑ In FY 2018 the target is to sequence over 9,000 isolates
- ❑ FSIS is exploring use of WGS beyond outbreak investigations and in FY 2018 forward FSIS will focus on understanding the occurrence, trend and patterns of genotypes of public health concern in FSIS regulated products
- ❑ In FY 2018 FSIS and partners received stakeholder input to understand the scope, applicability and perception, associated with the application of WGS in a regulatory setting
- ❑ FSIS continues to engage with National and International partners to stay at the cutting-edge of utilizing WGS technology
 - ❑ Work with National Antimicrobial Resistance Monitoring System (NARMS) partners (FDA, CDC) to understand the occurrence or introduction of antimicrobial resistance genes in pathogens and indicators
 - ❑ The WGS interagency collaboration Gen-FS charter was published in February 2018
- ❑ Note: In our investigative decision making we utilize WGS findings/interpretations - as a part of the totality of available evidence

Thank you!

*One Team, One Purpose -- Protecting Public
Health and Preventing Foodborne Illness*

Food Safety and Inspection Service
United States Department of Agriculture
www.fsis.usda.gov

USDA is an equal opportunity provider, employer, and lender.