Food Safety and Inspection Service

Whole Genome Sequencing (WGS) at FSIS: Current Status

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and

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Success = One-Team-One-Purpose

USDA

United States Department of Agriculture

One Team, One Purpose

Food Safety and Inspection Service

Protecting Public Health and Preventing Foodborne Illness

WGS at FSIS: Presentation Outline

- FSIS Mission and WGS
  - Mission Success and Challenge
- Current Application of WGS at FSIS
  - Outbreak Investigations, Antimicrobial Resistance (AMR), Harborage
- WGS Future at FSIS
- Healthy People 2020/2030
- Concluding Remarks

Food Safety and Inspection Service

WGS at FSIS: Our Authority and What We Do!

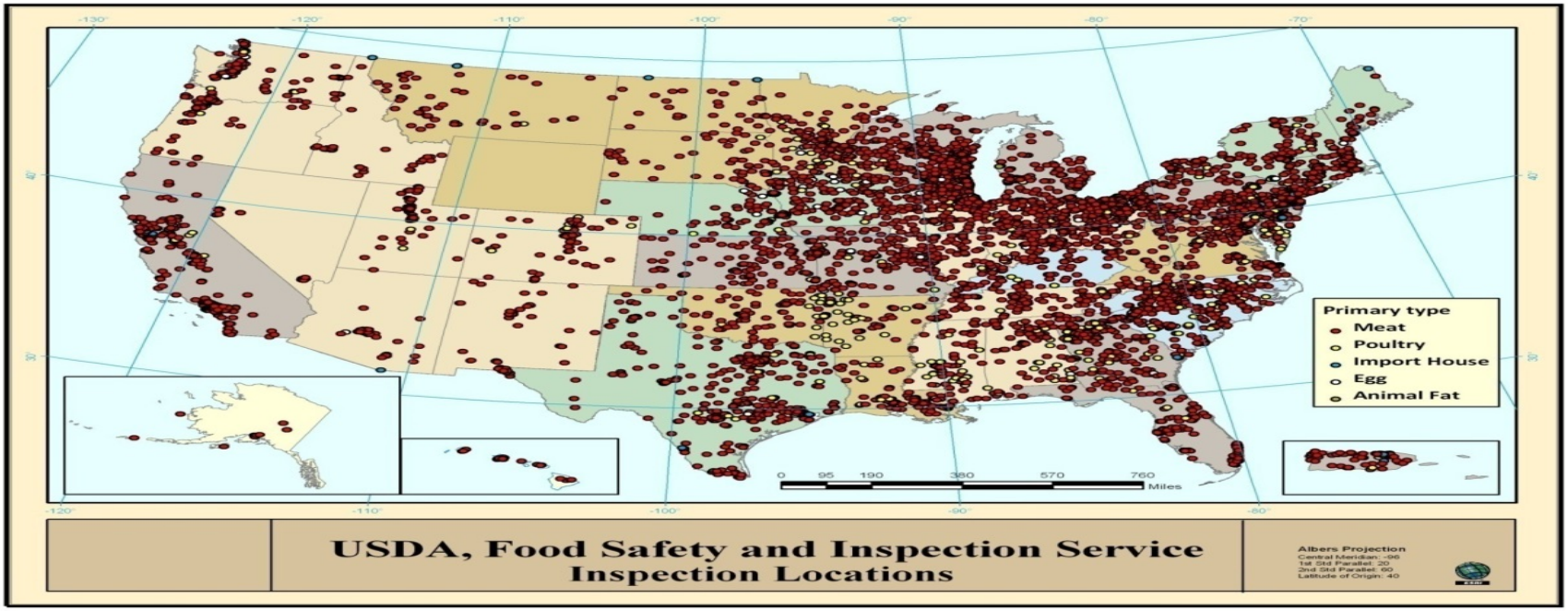
FSIS is the public health agency in the U.S. Department of Agriculture responsible for ensuring that the nation's commercial supply of meat, poultry, and egg products is safe, wholesome, and correctly labeled and packaged.

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

- **USDA Strategic Plan Goal 7**
  - **Provide all Americans access to a safe, nutritious, and secure food supply**

WGS at FSIS: Our Authority and What We Do!



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

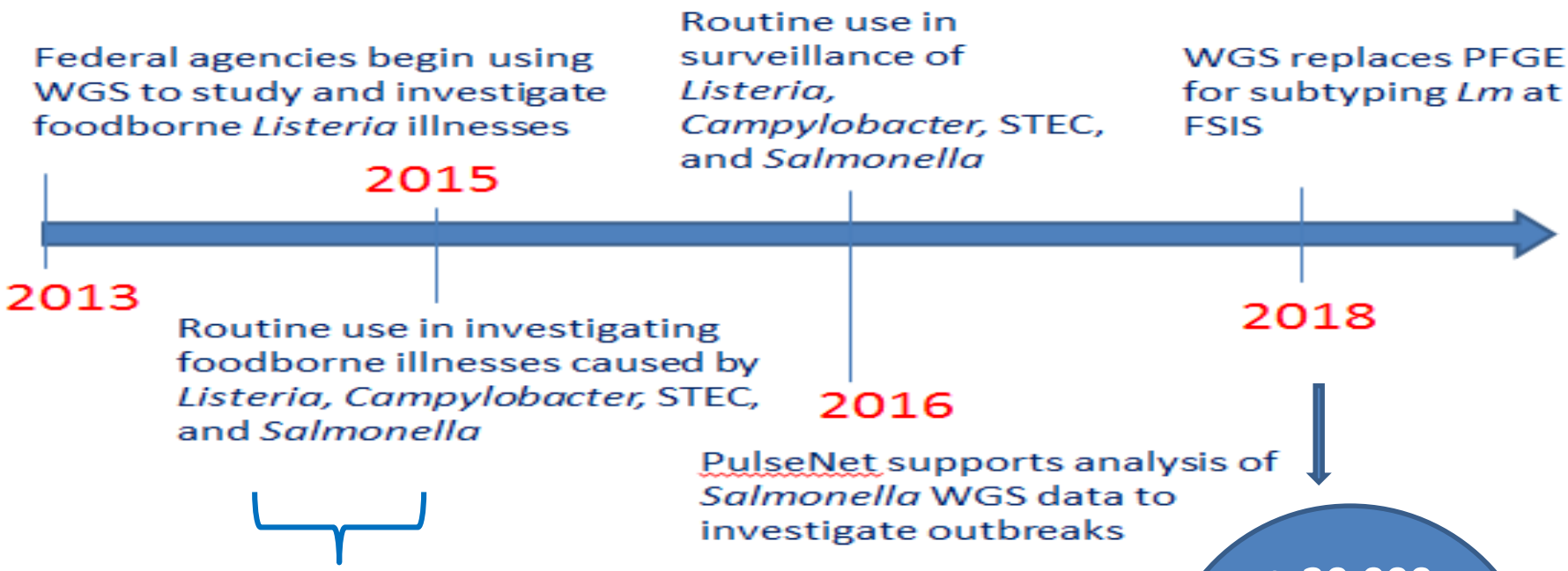
WGS and Analytics

Food Safety and Inspection Service:
WGS at FSIS: Strategic Plans and Application of Scientific Approaches

Continuous Application of Science and Technology at FSIS

Food Safety and Inspection Service

WGS at FSIS: Major Milestones



WGS in FSIS Lab System

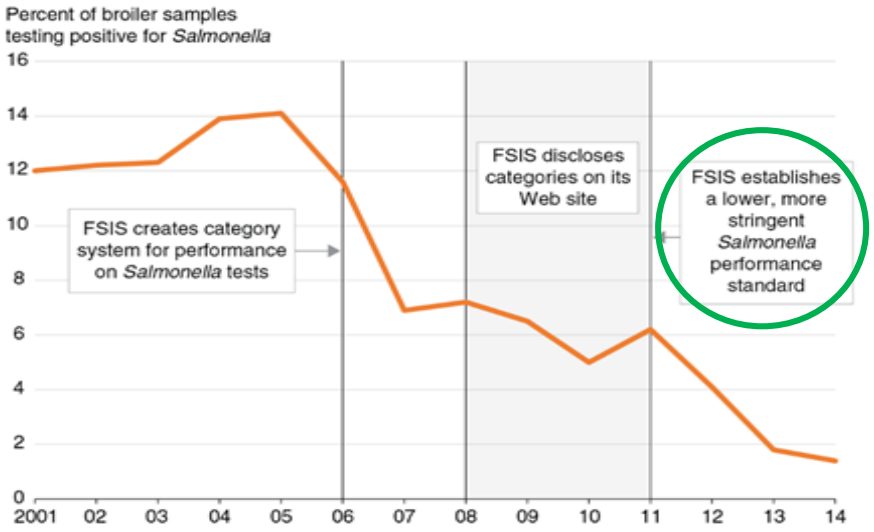
- ❑ July 2014: *Salmonella* and *Listeria monocytogenes*
- ❑ December 2014: STECs
- ❑ February 2015: *Campylobacter*
- ❑ May 2015: Capability to directly upload WGS files to NCBI

Food Safety and Inspection Service:
WGS at FSIS: Strategic Plans and Application of Scientific Approaches

Continuous Application of Science and Technology at FSIS

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

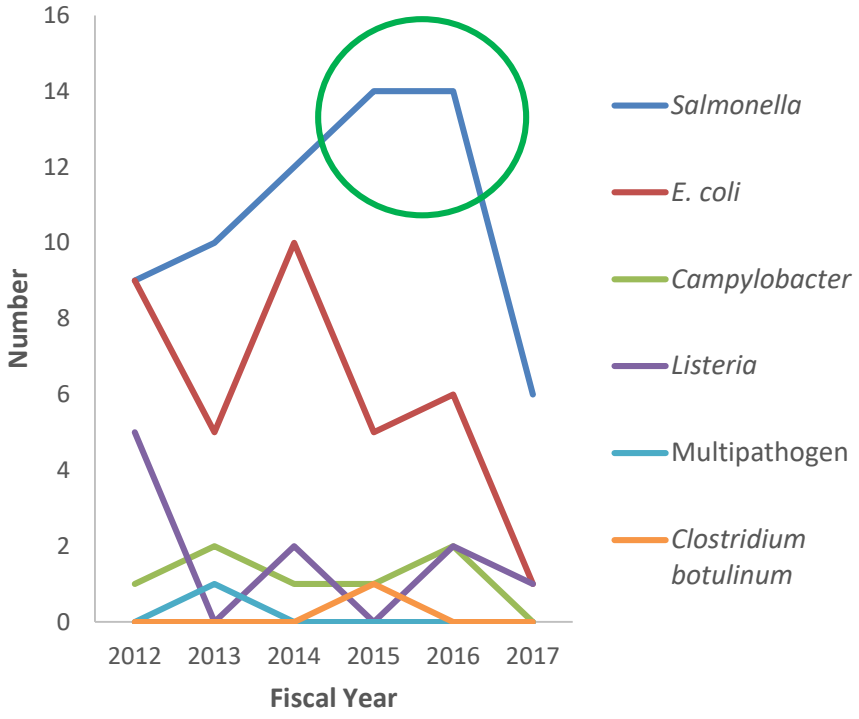


FSIS = Food Safety and Inspection Service.
Source: USDA, Economic Research Service using data from USDA, Food Safety and Inspection Service's Public Health Information System.

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)



WGS at FSIS: Application Considerations

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

❑ Focus on Genotypes

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

❑ Focus on Genes

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

Food Safety and Inspection Service:
WGS at FSIS: WGS in Outbreak Investigations

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

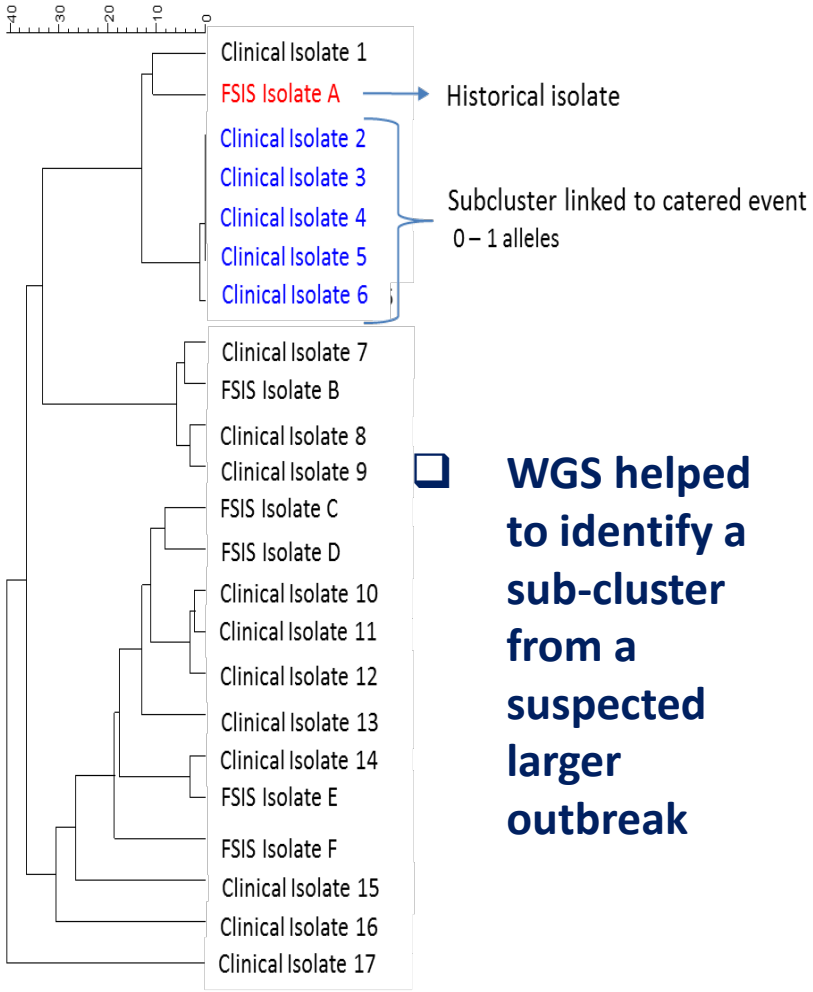
WGS was helpful in 4 outbreaks

- **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



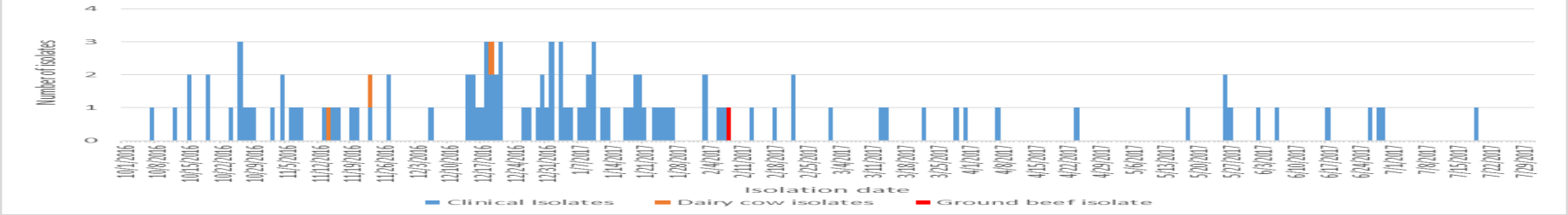
Annotated WGS Tree (Source: CDC)

- WGS helped to identify a sub-cluster from a suspected larger outbreak

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

WGS at FSIS: Utility of WGS to Determine Harborage

- **Harborage or Repeated Introduction:** When two or more closely related isolates are found in product, food contact, or non-food contact environmental samples that were collected over multiple days, weeks, months, or years
  - FSIS laboratories determine whether isolates are closely related using comprehensive information from different WGS tools
  - It is the establishment's responsibility to identify the underlying cause for harborage or repeated introduction, as a part of corrective actions
- **Dual Jurisdiction Establishments (DJEs):** These are establishments that produce both FDA and FSIS-regulated products
  - When one agency identifies potential harborage through bacterial characterization of *Lm* isolates (PFGE and/or WGS), information is shared to inform a collaborative regulatory response within the establishment
- **Note:** Even when isolates are determined to be genetically similar, additional evidence such as epidemiological data in outbreak investigations, is needed to confirm that isolates are a "match"

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

- 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 $bla_{\text{CTX-M-65}}$
  - Colistin Resistance
  - Quinolone Resistance
  - Linezolid Resistance

Healthy People Goals and Targets: 2020 → HP: 2030

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

- *Salmonella* Infantis with *bla*CTX-M-65 gene in a regulated product shows an upward trend from 2015 -2017
  - A single PFGE type was identified as containing a *bla*CTX-M-65 gene with distribution only six isolates in 2015
  - In 2016 the *bla*CTX-M-65 gene was seen in seven PFGE types and the isolates carrying this gene increased to 51
  - In 2017 the *bla*CTX-M-65 gene was seen in 22 PFGE types and the total isolates carrying this gene increased to 140

- Distribution of the *bla*CTX-M-65 gene among *Salmonella* Infantis Isolates from NCBI

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

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**
- ❑ **Healthy People 2030 Goals**
- ❑ **Opportunities for collaborations and data sharing**

WGS at FSIS: Where Do We Go From Here

WGS: Future

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)**

Food Safety and Inspection Service:
WGS at FSIS: Where Do We Go From Here

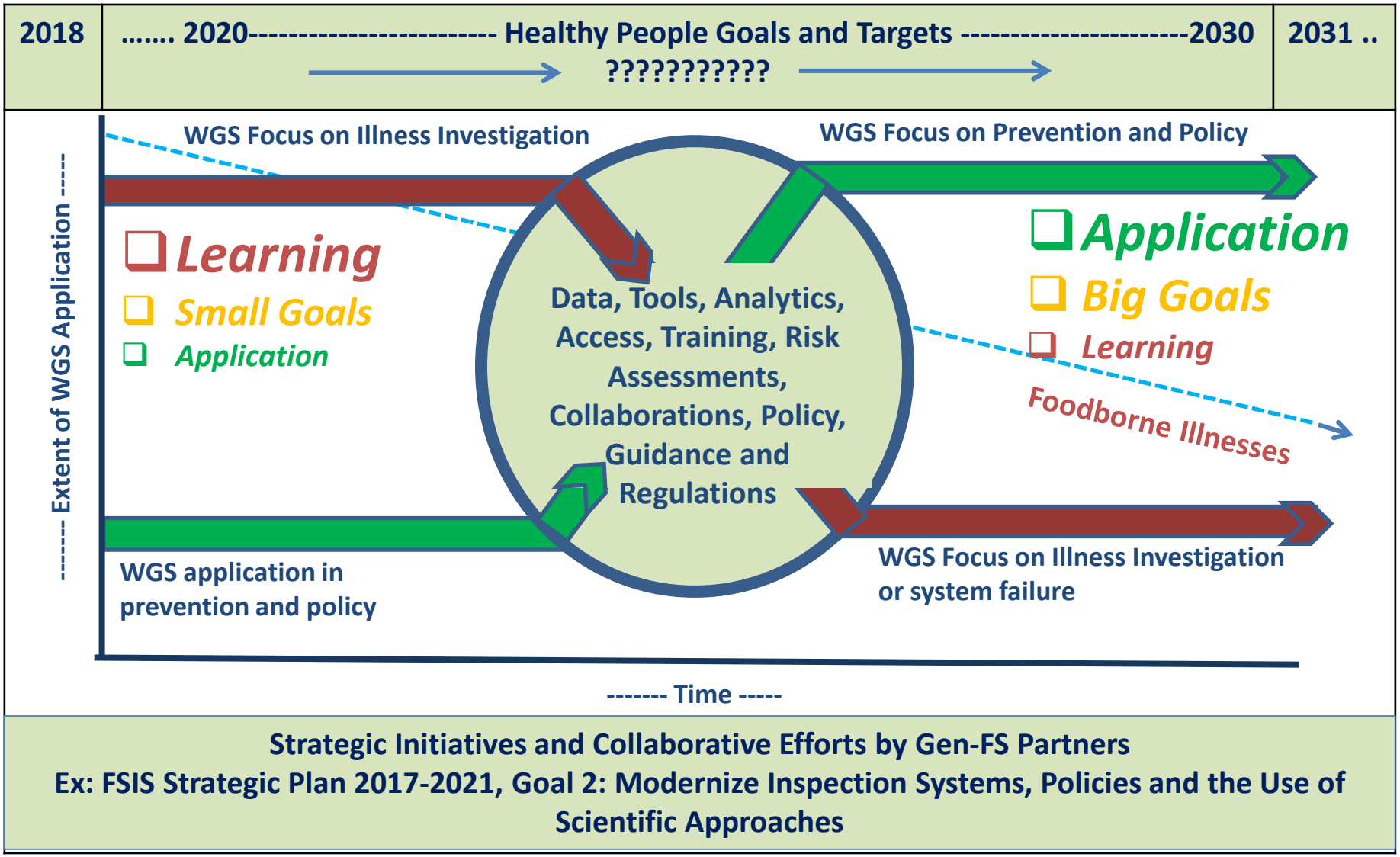
WGS: Future

Focus on Communication and Training

- ❑ **Standardize and simplify WGS related communications**
- ❑ **Communicating WGS results with regulated establishments**
- ❑ **Development/Availability of audience specific WGS training modules**
- ❑ **Continued engagement (Meetings, Webinars, FAQs etc.)**

Healthy People Goals and Targets: 2020 → **HP: 2030**

Food Safety and Inspection Service:
WGS at FSIS: Where Do We Go From Here: Healthy People 2030



Strategic Initiatives and Collaborative Efforts by Gen-FS Partners
Ex: FSIS Strategic Plan 2017-2021, Goal 2: Modernize Inspection Systems, Policies and the Use of Scientific Approaches

FSIS WGS Update: WGS - A Collaborative Undertaking

- FSIS - WGS Collaborations

U.S. Department of Health and Human Services

FDA U.S. FOOD & DRUG ADMINISTRATION

Illinois Institute of Technology

IFSH Innovation Through Collaboration INSTITUTE FOR FOOD SAFETY AND HEALTH

CDC Centers for Disease Control and Prevention

CDC 24/7: Saving Lives, Protecting People™

NCBI National Center for Biotechnology Information

USDA United States Department of Agriculture Food Safety and Inspection Service

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

WGS at FSIS: WGS at FSIS: Concluding Remarks

Continuous Application of Science and Technology at FSIS

External validation

FSIS Strategic Plan 2012 - 2016 → **Strategic Plan 2017 - 2021** → Strategic Plan 2022- 2026

- ❑ FSIS – A regulatory Agency
- ❑ Healthy People Goals (2020/2030) and pathogen Reduction challenges
- ❑ WGS Capacity at FSIS
- ❑ Application of WGS beyond current uses
- ❑ Public Meetings in FY 2018
- ❑ National and International partnerships
- ❑ Note: In our investigative decision making we utilize WGS findings/interpretations - as a part of the totality of available evidence

Healthy People Goals and Targets: 2020 → **HP: 2030**

- ❑ **USDA Strategic Plan Goal 7**
  - ❑ **Provide all Americans access to a safe, nutritious, and secure food supply**

Thank you!

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

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