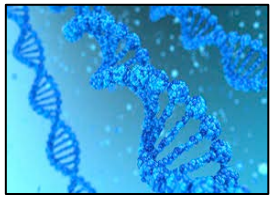
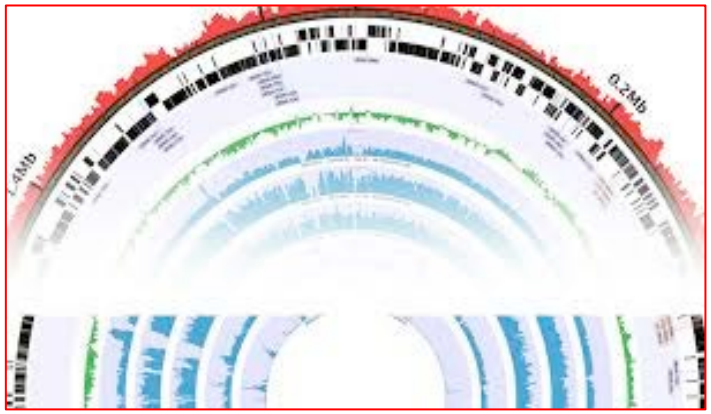


"How whole genome sequencing has transformed FDA's microbiological food safety program: Important highlights from the GenomeTrakr WGS Network"



Presented by:

Eric W. Brown, Ph.D., M.Sc., FAAM
Director, Division of Microbiology
&
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Senior International Liaison for Genomics and Food Safety
Office of International Engagement

Center for Food Safety & Applied Nutrition
U.S. Food & Drug Administration
College Park, MD 20740 USA

STAR-GAZING

LIGHT-TELESCOPE

MODERN REFRACTION TELESCOPE

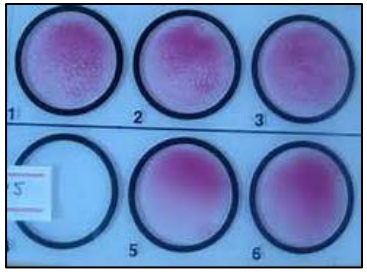
RADIO TELESCOPE

HUBBLE

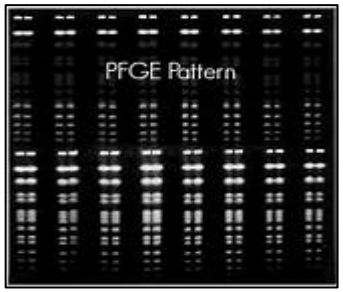
PATHOGEN PLATING

BIOTYPING SPECIATION

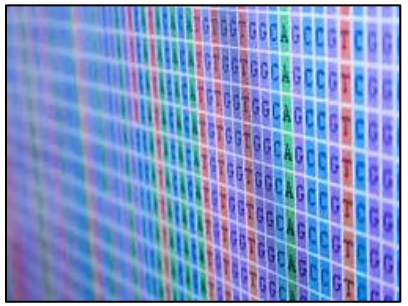
SEROTYPING



PFGE



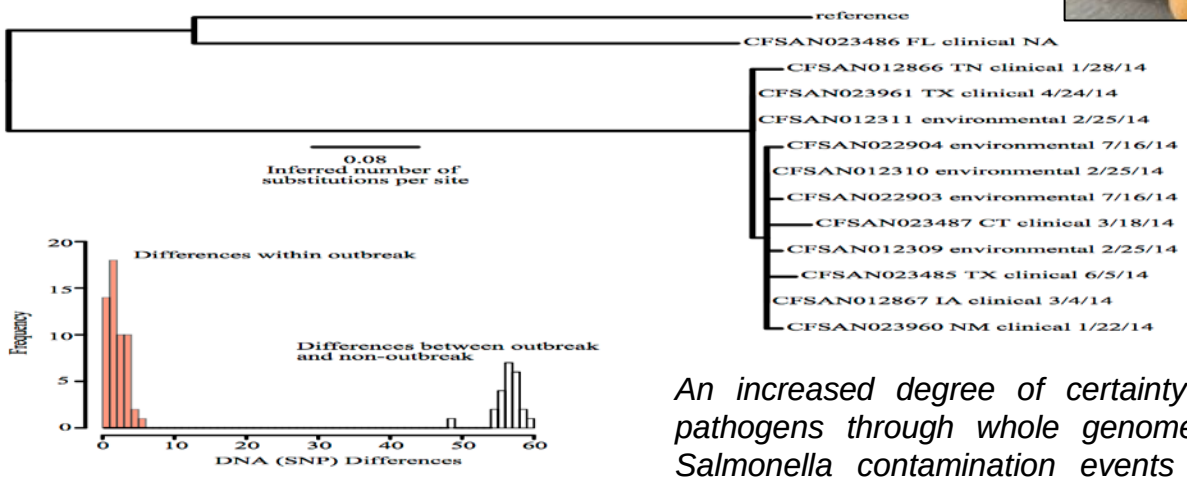
WGS



time

THE EVOLUTION OF SUBTYPING TOOLS FOR BACTERIAL PATHOGENS

Nut Butter Event



An increased degree of certainty that comes with matching strains of pathogens through whole genome sequencing allowed for detection of Salmonella contamination events across several states with low level contamination and widely distributed products.

Latin-Style Cheese Event

Same PFGE pattern 10-15 SNPs

outbreak 5 SNPs

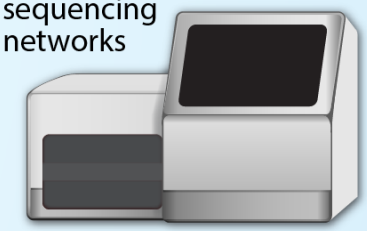
Basic Data Flow for Global WGS Public Access Databases

DATA ACQUISITION

Sequence and upload genomic and geographic data

GENOME TRAKR

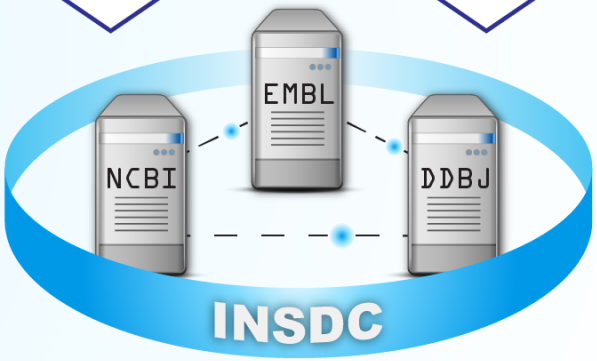
Other distributed sequencing networks



DATA ASSEMBLY, ANALYSIS, AND STORAGE

International Nucleotide Sequence Database Collaboration (INSDC)
Shared Public Access Databases

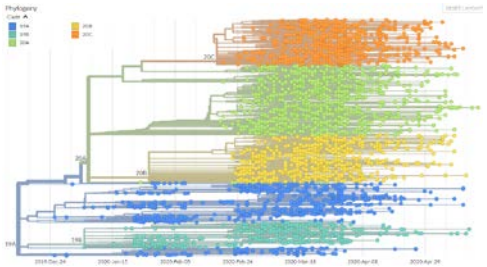
- *NCBI – National Center for Biotechnology Information*
- *EMBL – European Molecular Biology Laboratory*
- *DDBJ – DNA Databank of Japan*



PUBLIC HEALTH APPLICATION AND INTERPRETATION OF DATA

- *Find clinical links*
- *Identify clusters*
- *Conduct traceback*
- *Develop rapid methods*
- *Develop culture independent tests*
- *Develop new analytical software*

2-Part Paradigm Shift

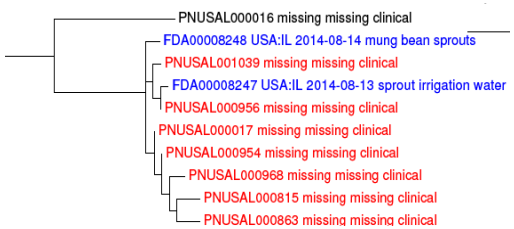


1. Whole Genome Sequencing
   - High-Resolution Data
   - Can infer evolutionary history of isolates
     - has this lineage been linked to a human/animal illness?
     - what are the sample sources of close relatives?
     - have we seen this same isolate in the same place in previous years, seasons?

2. Open Data – Even More Significant!
   - Raw genome sequences collected internationally and submitted to a public repository National Center for Biotechnology Information (NCBI).
   - Enables public/private partnership for collecting and analyzing data
   - GenomeTrakr/FDA isolates gain evolutionary/phylogenetic context when compared to the global contributors
     - Where did this clone/cluster emerge?
     - Does this outbreak extend beyond US borders?
     - Where and when did this ABC stress tolerance gene emerge?

2012-2014

New field: Genomic Epidemiology



Genomic signal

Epidemiological signal

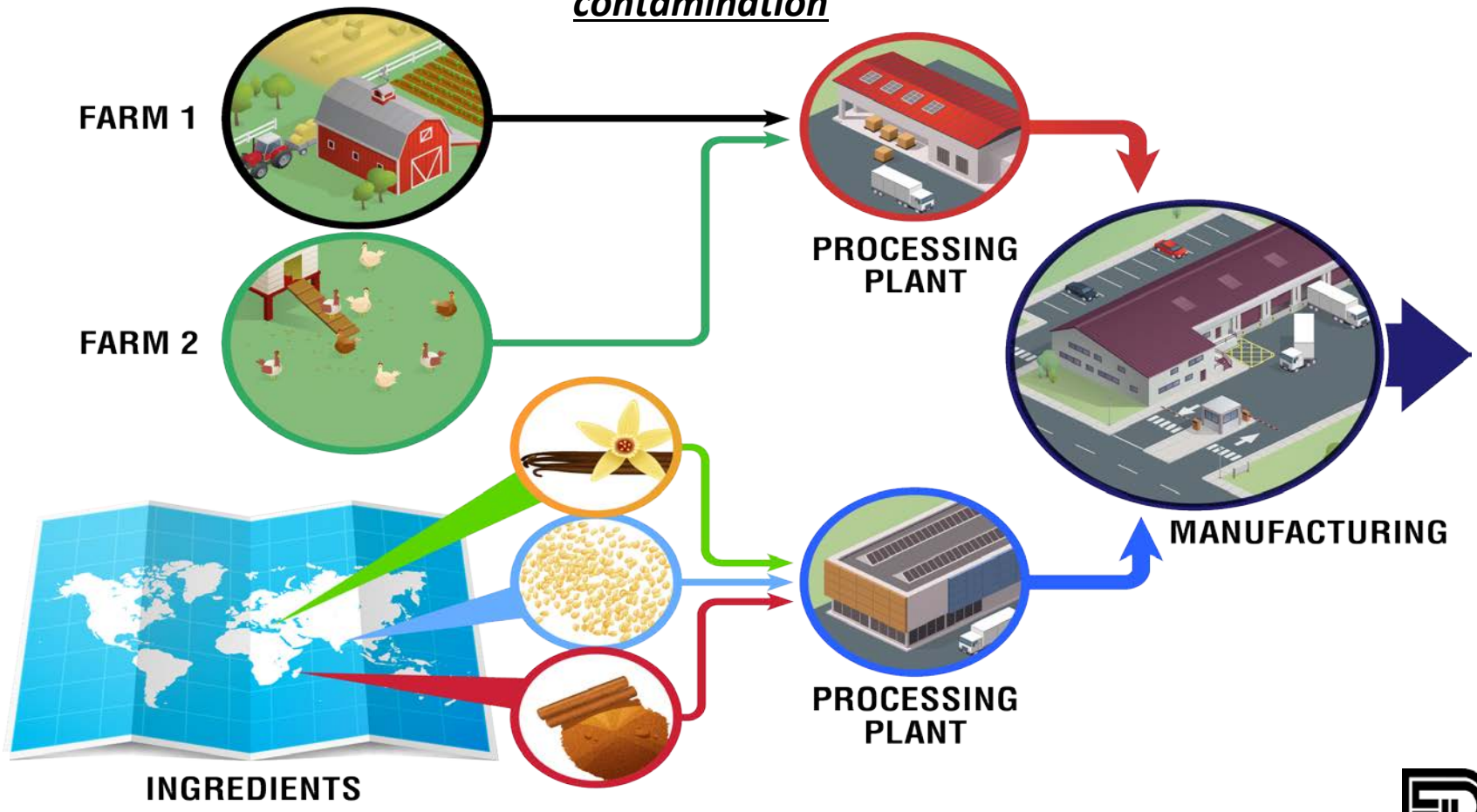
Traceback

Higher resolution WGS source tracking works.

- Fewer clinical cases needed to have confidence in cluster.
- Early & unambiguous determination of scope of cluster. Reduces false inclusion in cluster to improve statistics.
- Unrelated clinical isolates are evidence of independent co-occurring contamination, poly-clonality.
- Allows source tracking of previously indistinguishable serotypes.
- Higher confidence incentivizes early actions.

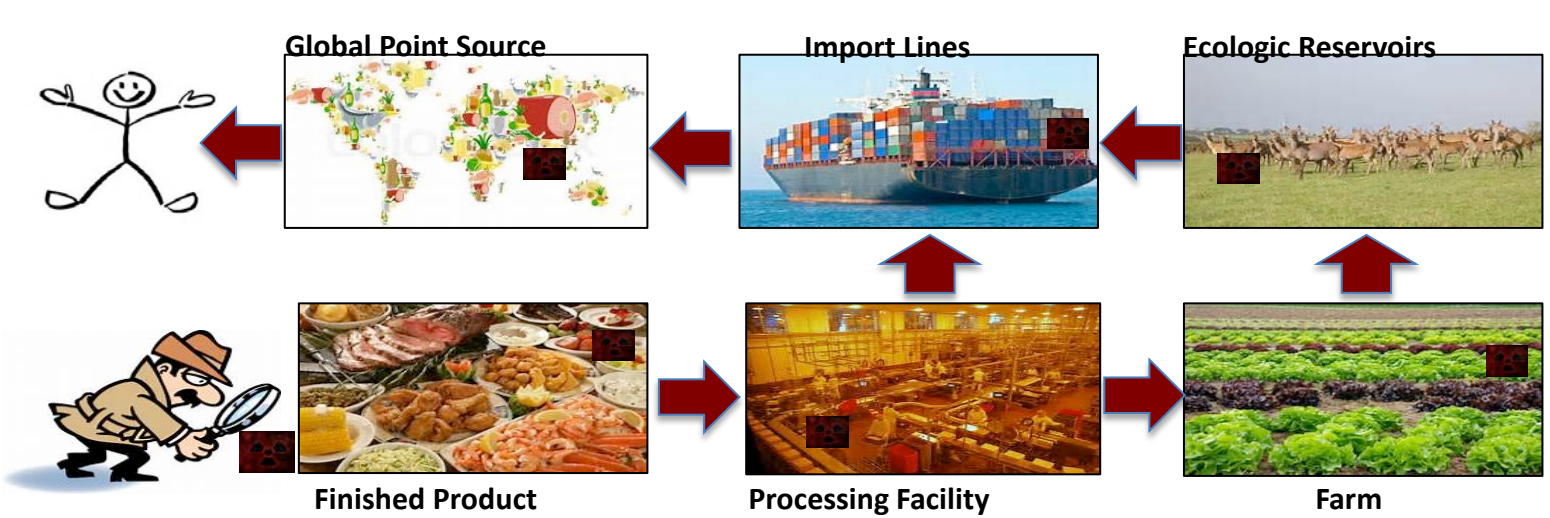
Support for Root Causes and Reservoirs

Environmental sampling combined with WGS can help point to root cause of the contamination



COMPLEX FOOD VEHICLES

(Slide courtesy of J. Ostell, NCBI)



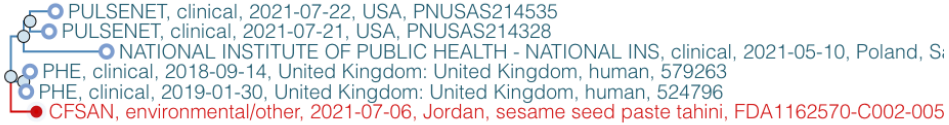
Salmonella tahini clusters highlight global contribution

103,465 Clusters currently tracked.

- United Kingdom (PHE)
- United States (GenomeTrakr, PulseNet)
- Canada (CFIA, NLM)
- Israel

- United Kingdom (PHE, GBRU)
- United States (GenomeTrakr, PulseNet)

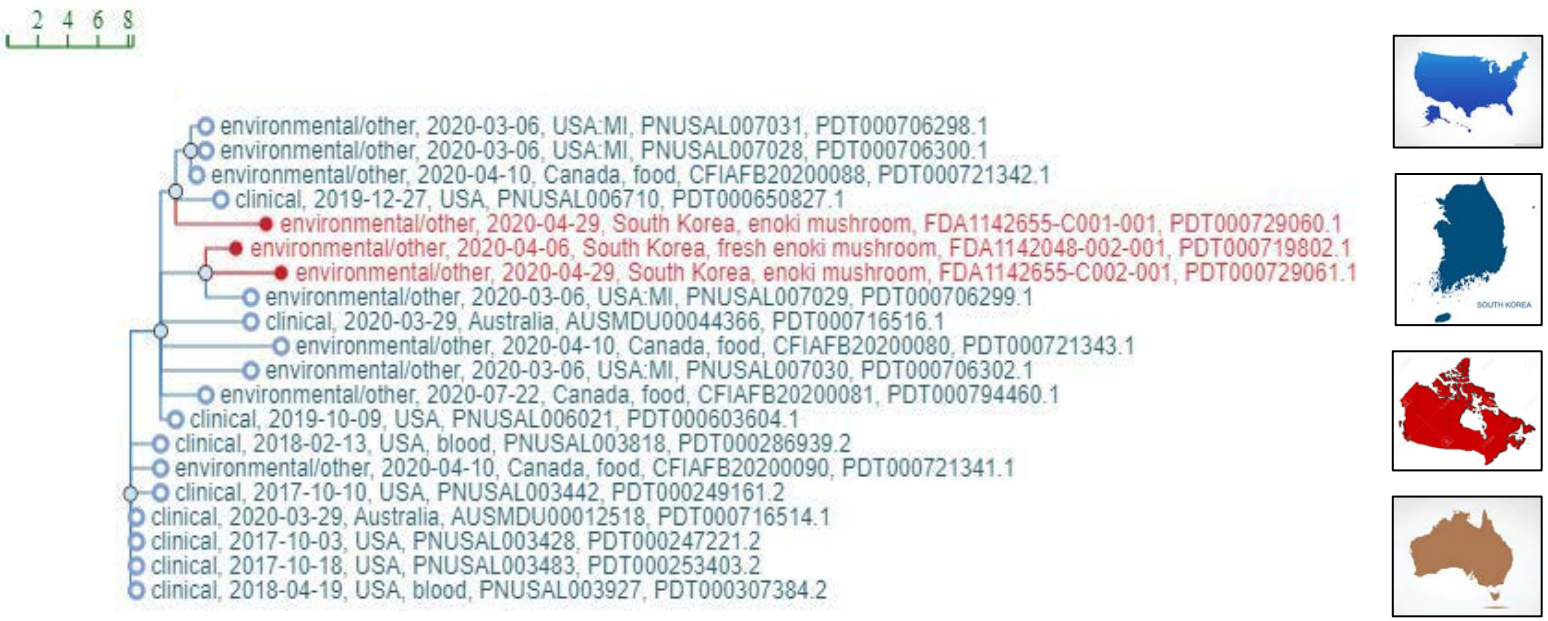
- United Kingdom
- United States (GenomeTrakr)



- United Kingdom (PHE)
- United States (GenomeTrakr, PulseNet)
- Poland

Listeria enoki mushroom event cluster highlights global NGS contribution

103,465 Clusters currently tracked.



Looking ahead

- Data Integrity
- Capacity building – hardware, software and people
- Sharing of WGS data and metadata
- Rapid movement away from alternative typing methods
- Bioinformatics –
  - Analysis – Cloud based on Galaxy
  - “Hands on” – Training videos
  - NCBI - https://www.ncbi.nlm.nih.gov/pathogens/

Document type: International standard
Document subtype: if applicable
Document stage: (19) Preparation
Document language: E
Chair: Errol Strain, Ph.D. (US FDA)

Reference number of working document:
ISO/TC 34/SC 9 N 2133
Date: 2018-01-29
Reference number of document:
Committee identification: ISO/TC 34
Secretariat: ANSI

Microbiology of the Food Chain — Genomic sequencing of foodborne microorganisms — General requirements and guidance for bacterial genomes

MINIMAL STANDARDS FOR:

Coverage/Data Quality/Chemistry/Alignment Parameters/Data Translation (SNP or Allele Calling)/Clustering Tools/Data Interpretation and Linkage

DM ISO and WGS Leads Finalized and Helped to Ratify the Global Whole Genome Sequencing Standard "ISO/DIS 23418 Microbiology of the food chain – Whole genome sequencing for typing and genomic characterization of foodborne bacteria"

International Organization for Standardization

Genomics Brings the World of One Health into a Manageable Light

GENOME TRAKR

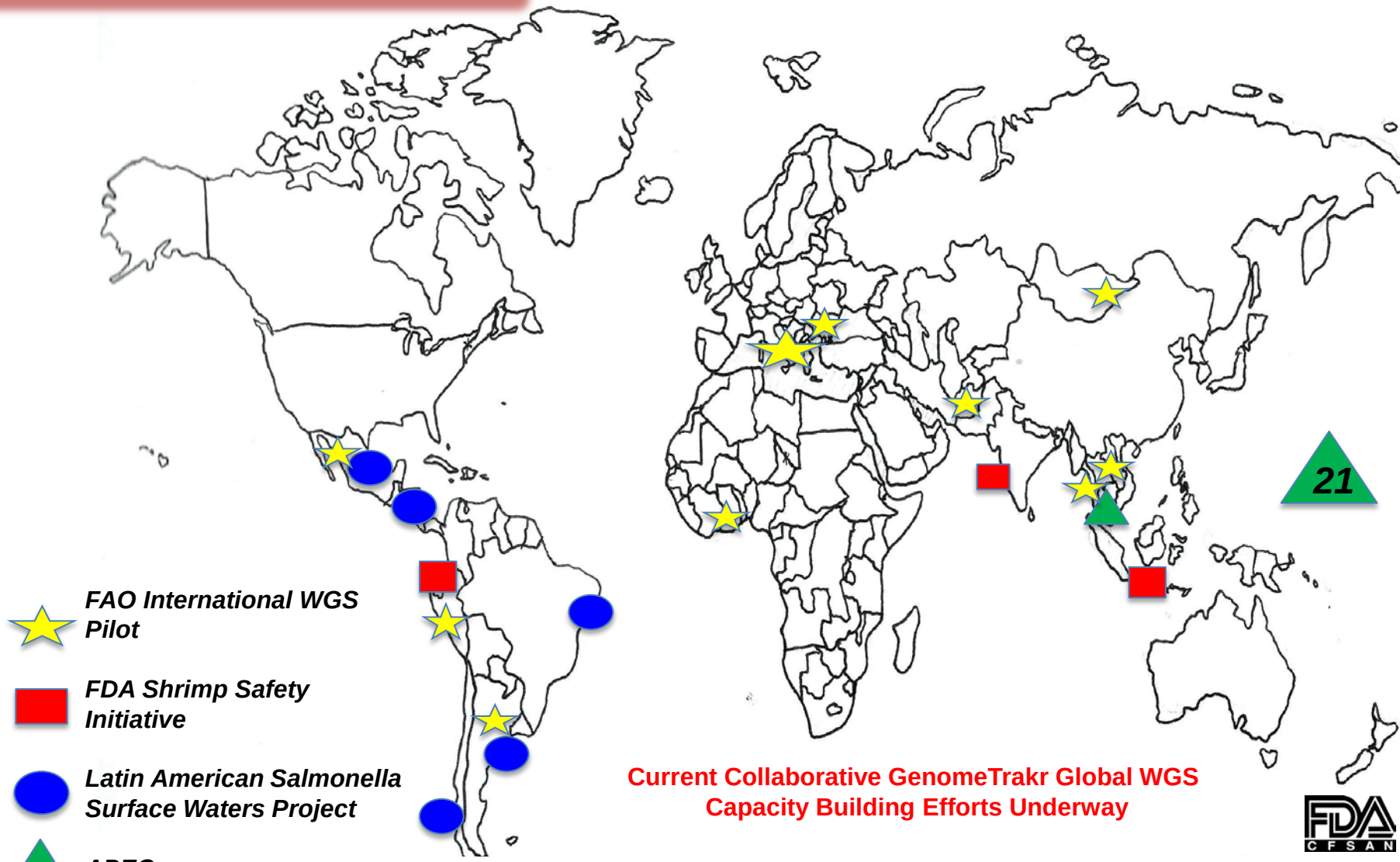
FDA CFSAN

GLOBAL WATER & FOOD SAFETY SUMMIT

Increase environmental sampling across the US, and abroad.
Meeting Nov. 19 - 21, 2019 College Park, MD and FAO, Rome, 2024

FDA

International WGS Capacity Building

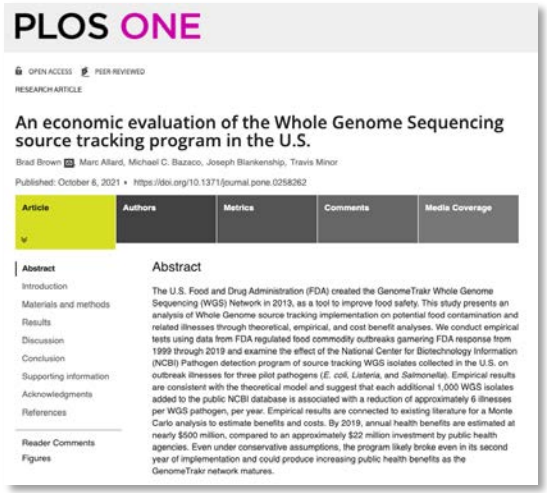


Current Collaborative GenomeTrakr Global WGS Capacity Building Efforts Underway

FDA CFSAN

Economic Impact

- GenomeTrakr program was likely cost effective by its second year of implementation
- $100 M -> $450 M in net annual health benefits (est. from 2019). >$ Billion estimated benefits.



PLOS ONE

OPEN ACCESS PEER-REVIEWED

RESEARCH ARTICLE

An economic evaluation of the Whole Genome Sequencing source tracking program in the U.S.

Brad Brown, Marc Allard, Michael C. Bazaco, Joseph Blankenship, Travis Minor

Published: October 6, 2021 • https://doi.org/10.1371/journal.pone.0258262

Article | Authors | Metrics | Comments | Media Coverage

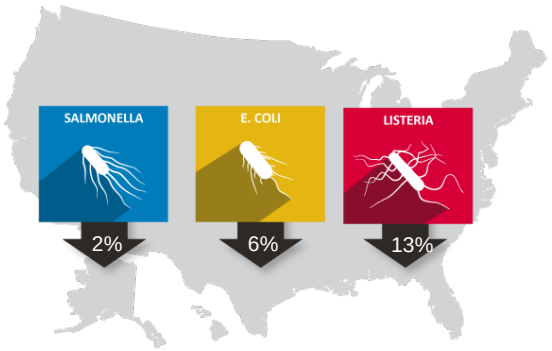
Abstract

Introduction
Materials and methods
Results
Discussion
Conclusion
Supporting information
Acknowledgments
References

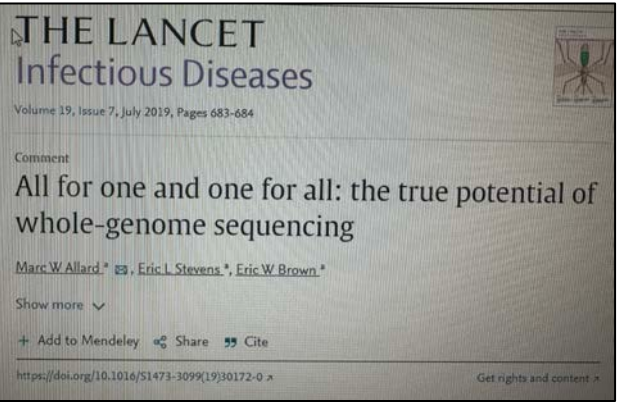
Reader Comments
Figures

Abstract

The U.S. Food and Drug Administration (FDA) created the GenomeTrakr Whole Genome Sequencing (WGS) Network in 2013, as a tool to improve food safety. This study presents an analysis of Whole Genome source tracking implementation on potential food contamination and related illnesses through theoretical, empirical, and cost benefit analyses. We conduct empirical tests using data from FDA regulated food commodity outbreaks garnering FDA response from 1999 through 2019 and examine the effect of the National Center for Biotechnology Information (NCBI) Pathogen detection program of source tracking WGS isolates collected in the U.S. on outbreak illnesses for three pilot pathogens (*E. coli*, Listeria, and *Salmonella*). Empirical results are consistent with the theoretical model and suggest that each additional 1,000 WGS isolates added to the public NCBI database is associated with a reduction of approximately 6 illnesses per WGS pathogen, per year. Empirical results are connected to existing literature for a Monte Carlo analysis to estimate benefits and costs. By 2019, annual health benefits are estimated at nearly $500 million, compared to an approximately $22 million investment by public health agencies. Even under conservative assumptions, the program likely broke even in its second year of implementation and could produce increasing public health benefits as the GenomeTrakr network matures.



Return on Investment: $10 dollars in averted human health costs for every $1 dollar invested. For each additional 1,000 WGS isolates added to the public NCBI database is associated with a reduction of approximately 6 illnesses per WGS pathogen, per year.



www.fda.gov

WGS Surveillance Outcome

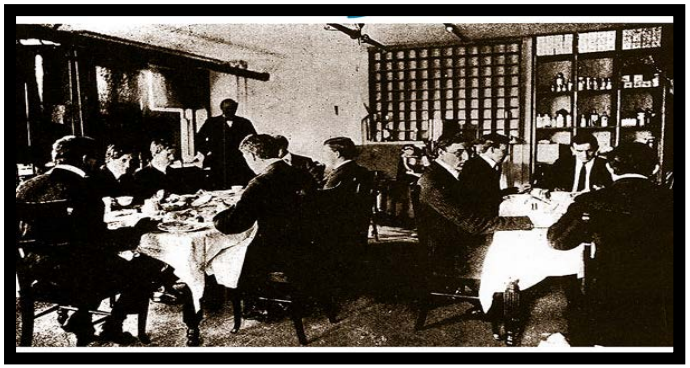
Increased use of WGS

More outbreaks identified

Fewer Sick People

Illness Averted

Genome sequences are portable and instantly cross-compatible. One technology approach irrelevant of organism or country or region. A single agnostic way to drive one-health around the globe.



FDA circa 1906 –The Poison Squad

11 years and growing

- **FDA**
  - Center for Food Safety and Applied Nutrition
  - Center for Veterinary Medicine
  - Office of Regulatory Affairs
- **National Institutes of Health**
  - National Center for Biotechnology Information
- **State Health and University Labs**
  - Alaska
  - Arizona
  - California
  - Florida
  - Hawaii
  - Maryland
  - Minnesota
  - New Mexico
  - New York
  - South Dakota
  - Texas
  - Virginia
  - Washington

- ***GenomeTrakr STAKEHOLDERS (National and international)***
- *FDLI, GMA, VA FSTF, CDC, FBI, PULSENET-LATIN AM., AM. ACAD MICROBIOL, ASM, FSIS, ARS, UNIV VERMONT, MINN DOH, AZ DOH, UNIV FL, VA DOH, WA DOH, TX DOH, NY AG LAB, IRISH FSA, NOVA SE UNIV, IGS BALTIMORE, INFORM MEETING, HONGKONG POLYT U, NIST, ITALIAN FSA, EFSA, WHO-FOOD SAFETT DIR, WHO-GFN, CDC-EU, EMERGING INFECTIOUS DIS CONF, DANISH TECH UNIV, NM STATE UNIV/ NM DOH, CARLOS MALBRAN INST/ARG, ST COULD UNIV/FOOD MICRO, SENASICA, GMI, NY DOH/WADSWORTH CENT, UNIV HAMBURG, CHINA CDC, NESTLE, FERA-UK, MD DOH, IAFP, APHL, AFDO, BELGIUM, VA Tech, US ARMY, US NAVY, MELBOURNE FSA (AUS), UNIV NEBRASKA, PUBLIC HEALTH ENGLAND, DHS, DELMARVA TASKFORCE, PENN STATE FOOD SCIENCE, PROD MAN ASSOC, ILLUMINA, UNIV IRELAND/DUBLIN COLLEGE, NCBI/NIH, GSRS GLOBAL SUMMIT, FAO/OIE, PUBLIC HEALTH CANADA, CFIA, HEALTH CANADA, INTL VTEC MEETING, CPS-GA, AOAC, UNITED FRESH, COLUMBIA, HAWAII DOH, CA DOH, ALASKA DOH, SOUTH DAK UNIV, UNIV GA, UNIV IOWA/DOH, UNIV CHILE, BRAZIL, OSU VETNET, TURKEY, MEXICO, IEH, SILLAKER, NEW ENG BIOLAB, PACIFIC BIO, CLC-BIO/QIAGEN, CON-AGRA, DUPONT, AGILENT, UC-DAVIS, HARVARD MED, INFORM MEETING, THAILAND, SINGAPORE FOOD SAFETY AUTHORITIES*

Intra-Agency Partners

ORA, OCC, OFS, OC, OAO, OFVM/SRSC, CFSAN, CDER, CBER, CDRH, CVM, NCTR, FDA CHIEF SCIENTIST, OIP, OARSA, SCIENCE BOARD, IAS, FFC, FERN, JIFSAN ADVISORY COMMITTEE, IFSH, MOFFETT CENTER CIO, DAUPHIN ISLAND, CFSAN-OCD, CORE, WESTERN CENTER.

- **USDA/FSIS**
  - Eastern Laboratory
- **CDC**
  - Enteric Diseases Laboratory
- **INEI-ANLIS "Carolos Malbran Institute," Argentina**
- **Centre for Food Safety, University College Dublin, Ireland**
- **Food Environmental Research Agency, UK**
- **Public Health England, UK**
- **WHO**
- **FAO**
- **APEC**
- **JIFSAN**
- **Illumina**
- **Pac Bio**
- **CLC Bio**
- **Other independent collaborators**