NDIA Conference Presentation

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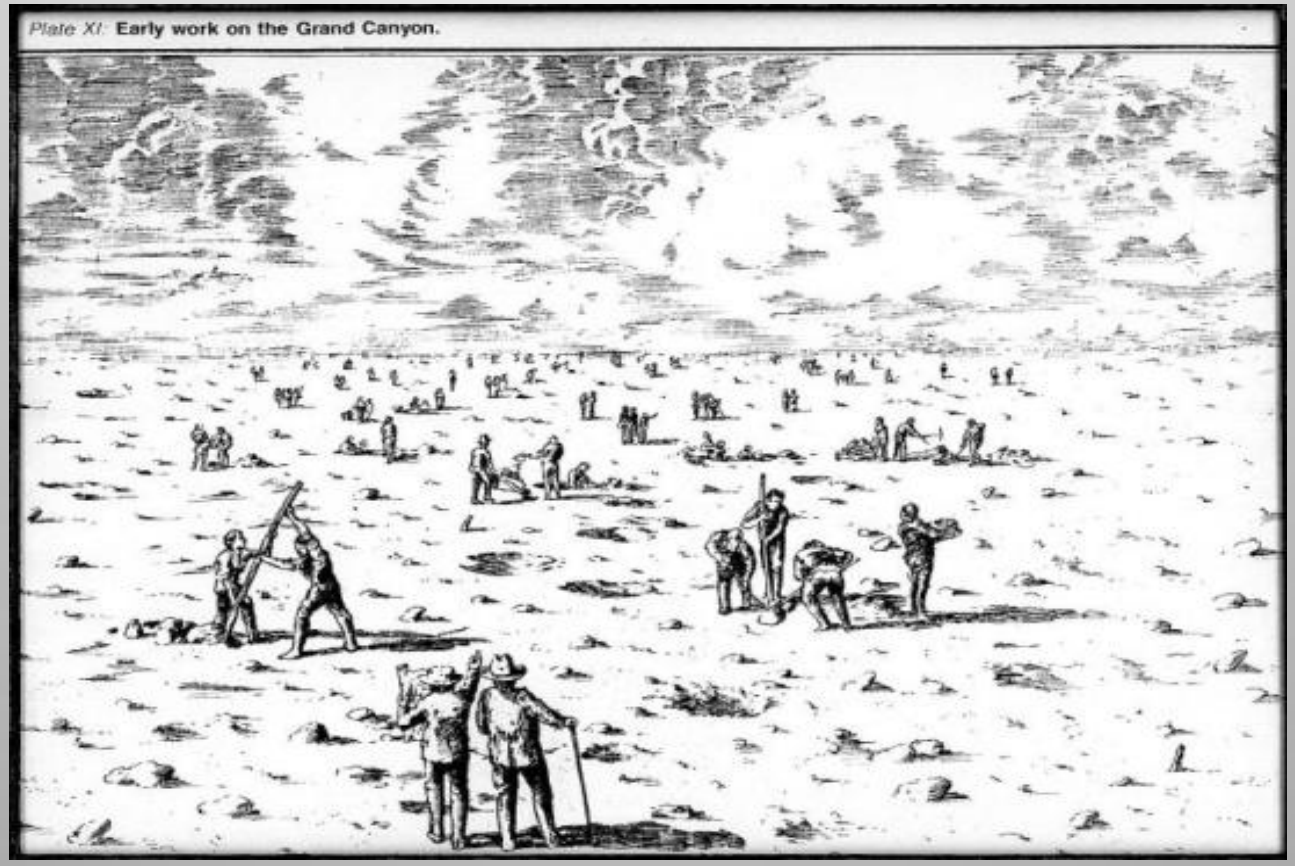
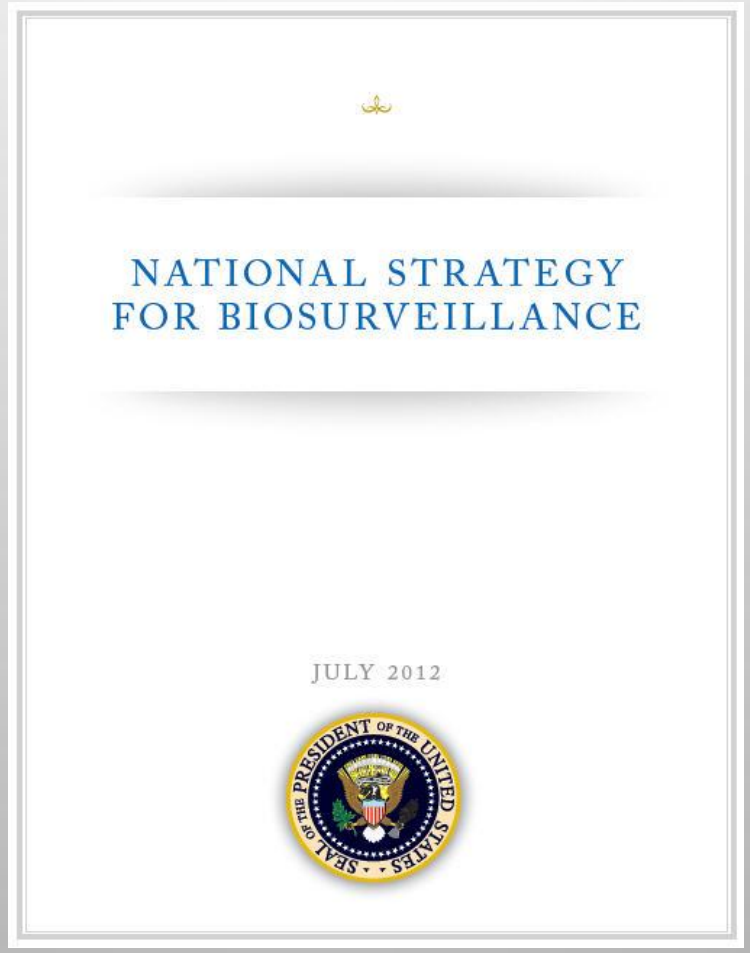
Early work on the Grand Canyon: The Daunting Cultural, Political, and Technical Hurdles Slowing the Definition, Design, and Implementation of an Effective "One Health" Biosurveillance System



NOW WE HAVE A STRATEGY…



The Strategy isn't very specific…

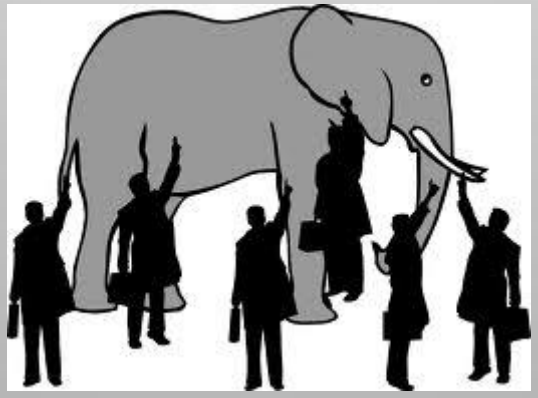
- Guiding Principles
  - Leverage Existing Capabilities
  - Embrace an All-of-Nation Approach
  - Add Value for All Participants
  - Maintain a Global Health Perspective
- Biosurveillance Goal and Core Functions
  - Scan and Discern the Environment
  - Identify and Integrate Essential Information
  - Alert and Inform Decisionmakers
  - Forecast and Advise Impacts
- Enablers for Strengthening Biosurveillance
  - Integrate Capabilities
  - Build Capacity
  - Foster Innovation
  - Strengthen Partnerships

Some Excerpts from the Strategy

- The goal is to achieve a well-integrated national biosurveillance enterprise that saves lives by providing *essential information* for better decisionmaking at all levels.
- We must be resolved to strengthen life-saving biosurveillance capabilities **within our existing resources**. We can do this by leveraging more effectively our existing national network of expertise and capabilities, and through targeted enhancements that provide benefits across the enterprise.
- The approach builds on existing biosurveillance concepts and capabilities in seeking to enable more rapid detection, knowledge, and characterization of human, animal, or plant disease activity to enhance incident situational awareness.

How is Biosurveillance Defined by the Strategy?

- The Strategy defines biosurveillance as the process of gathering, integrating, interpreting, and communicating essential information related to all-hazards threats or disease activity affecting human, animal, or plant health to achieve early detection and warning, contribute to overall situational awareness of the health aspects of an incident, and to enable better decision-making at all levels.



Other definitions are in use today…

- **What do *you* mean by "Biosurveillance"?**
  - **Reportable diseases information trickling in weeks after the fact?**
  - **Monitoring social media?**
  - **Monitoring ProMed Mail, Argus, FluNet, HealthMap, etc.?**
  - **Syndromic surveillance? (e.g., monitoring over the counter flu remedy sales, etc.)**
  - **Use of improved diagnostics on human/animal/plant hosts?**
  - **Regular monitoring of environmental reservoir hosts and vectors?**
  - **Zoonotic disease monitoring (e.g., migratory birds, etc.)?**
  - **Assisting other countries to more rapidly identify novel outbreak strains?**

The Strategy ducks some sensitive issues…

How did we get into this situation and what are the biggest impediments to getting needed progress?

WHAT PROBLEMS DOES THE STRATEGY AIM TO FIX?

- We aren't gathering the right information
- We aren't properly sharing the information we do have
- We aren't using available technologies well
  - Food and product safety are in poor shape
  - Human health care slow to adopt technologies to better diagnose disease and drug resistance
  - We aren't harnessing social media properly to obtain early warning of unusual events
- We don't have sufficient human or environmental baseline data

We really aren't ready for disasters, natural or otherwise.

Let's take a quick look at a few of the problems that need to be addressed

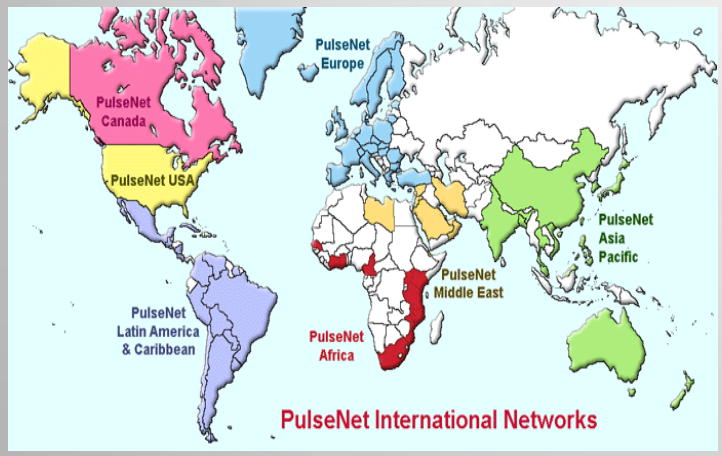
I'll only comment on a few areas where I have personal observations.

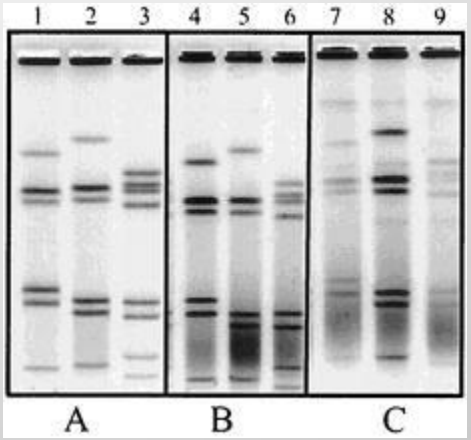
Biosurveillance is inherently a global problem…anthrax is just a minor part

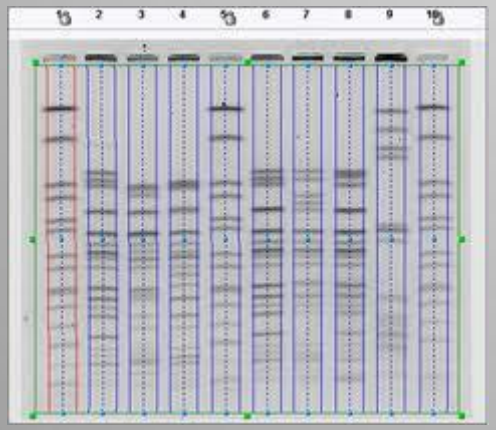
Is Environmental Surveillance the useless failure some say it is?

Our BioWatch experience say no…

The 1980's technique used for genotyping food pathogens has only ~20Kbp resolution.



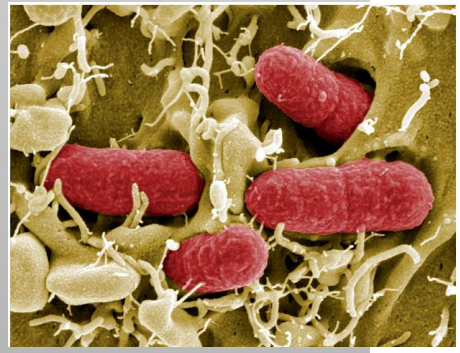


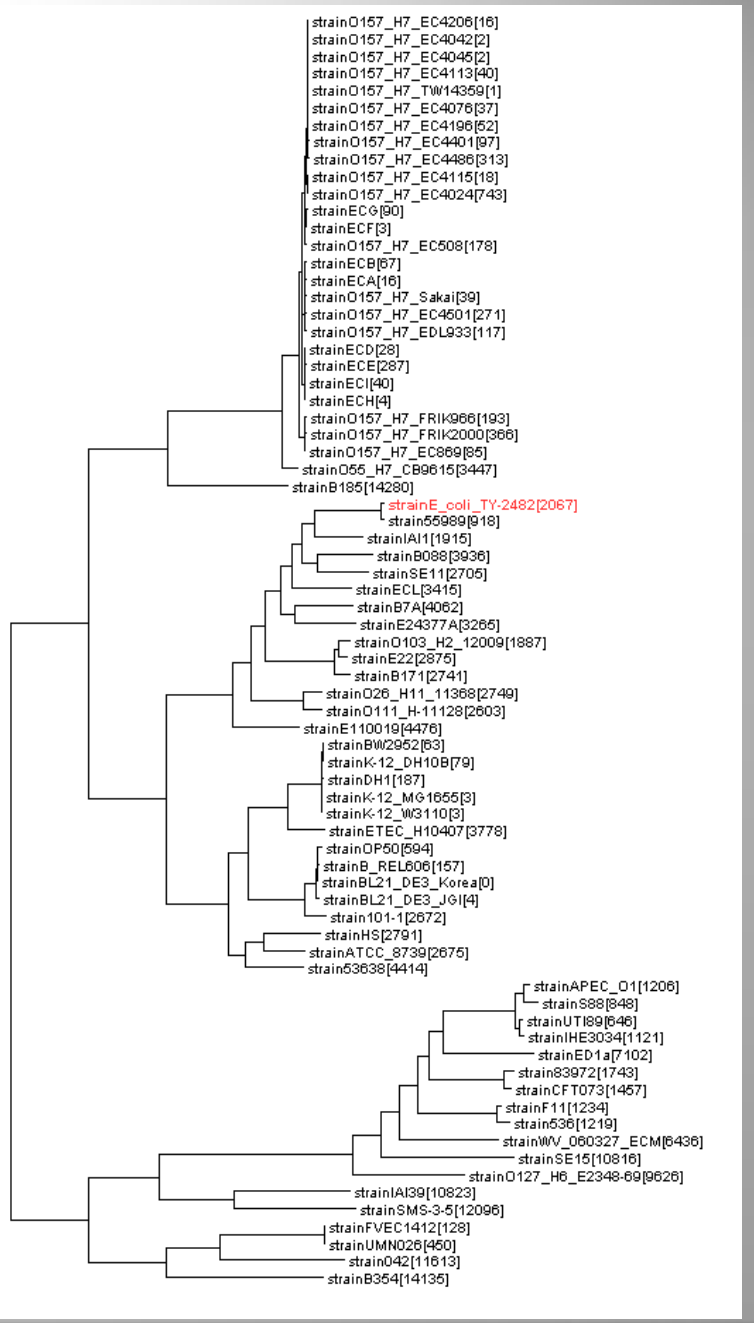


1980's low-cost technology will be hard to supplant with modern 1bp-resolution methods

SNP 1bp resolution: 2011 *E. coli* outbreak

- TY-2482 strain from May-June 2011 Germany outbreak
- Analyzed raw reads or assembled contigs, together with 73 available finished and draft *E. coli* genomes
- Found 367,059 SNP loci across all *E. coli* genomes; 2067 that differentiate TY-2482 uniquely
- Analyses completed in a few hours
- **Raw reads gave identical results as the assembled contigs.**
- **No assembly required!**





How much did the CDC spend on bioinformatics in 2010?

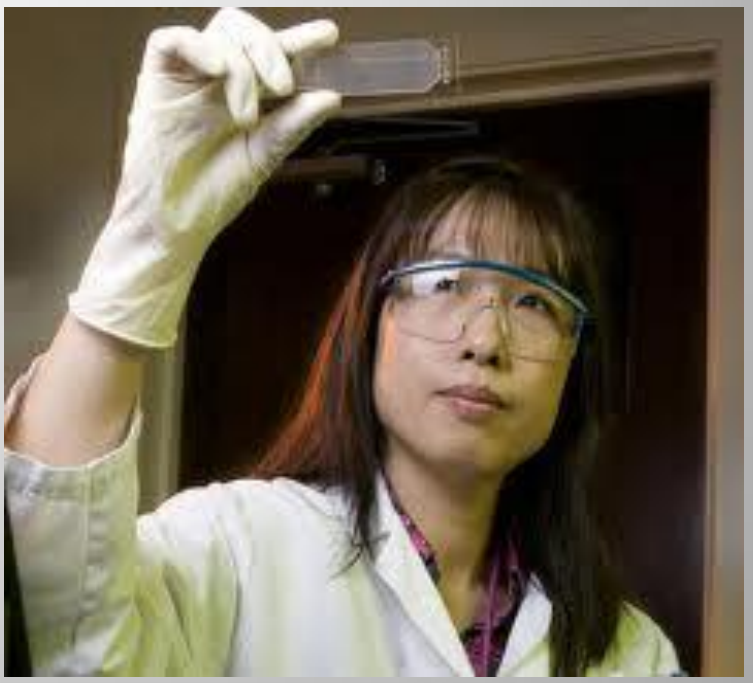
Federal agencies in general are short on bioinformatics

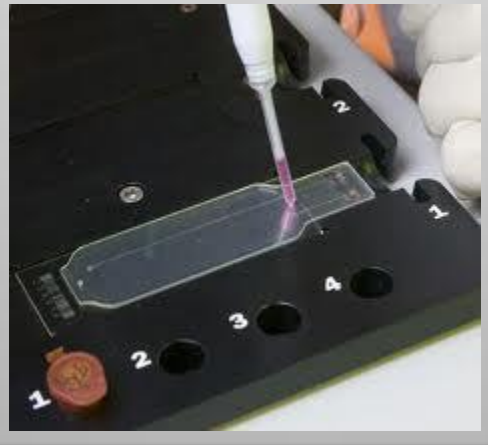
- Federal salaries are non-competitive for this high-demand specialty
- Our medical system and many agencies are led by old-school epidemiologists who were not trained in modern molecular methods
  - A generational change will be required to diagnose pathogens instead of treating symptoms
    - — Physicians and researchers who grew up with high-resolution molecular diagnostic methods

Data generation has far out-stripped data analysis

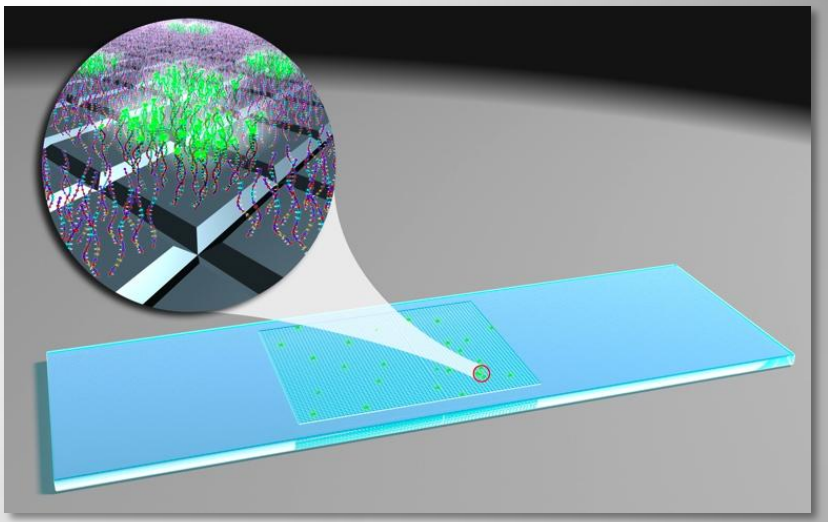
How hard is it to get FDA validation for a highly-multiplexed diagnostic?

(HINT: This is another trick question.)





Microbial Detection Array

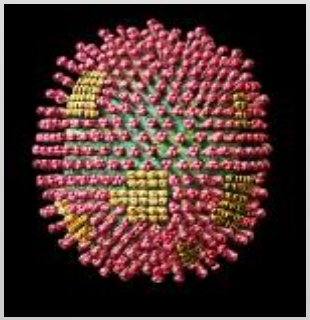


5,700+ sequenced microbial species

- 3,179 viral species
- 2,223 bacterial species
- 136 fungal species
- 124 archaea species
- 96 protozoa

387,156 total probes

- Probes are 50-65 bases long
- Unique regions from microbial species used



A Microbial Detection Array (MDA) for Viral and Bacterial Detection. Gardner SN, Jaing CJ, McLoughlin KS, Slezak TR. *BMC Genomics* 2010, **11:**668doi:10.1186/1471-2164-11-668, published Nov 25, 2010.

Enabled by Bioinformatics

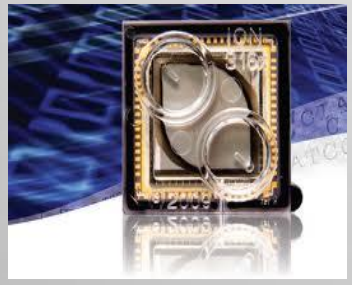
- Expertise in DNA signatures and biostatistics
- Computing power

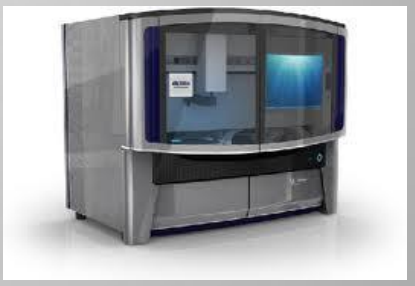
Good news: FDA working hard to define workable validation plan for multipathogen assays

- DTRA leading an effort to help FDA define and populate the reference database(s) needed to support increased *in slilco* validation for sequence-based assays
- NCBI is actively involved to house the reference database
- Other relevant Federal agencies are being invited to participate

Great example of a bottom-up inter-agency effort

DNA sequencer evolution and biosurveillance needs: how well matched?





Driven by human genome re-sequencing

Is DNA sequencing the answer to all human diagnostic questions?

- Even if sequencing were instantaneous and free, the cost of data analysis, storage, and interpretation remains substantial
- For known pathogens, why re-sequence an individual's 3Gbp genome to locate the 20Kbp virus that is making them ill?
- Direct detection of pathogens via sequence-based assays (e.g., multiplex-PCR, microarrays, etc.) will remain viable, especially when scaled for routine use

When did all the Federal agencies turn into “small science” clones?

- Biosurveillance is clearly a “Big Science” problem
- You can’t solve it with 5,000 single-investigator grant awards…
- Most agencies lack Big Science management experience
- Biosurveillance is too Balkanized to make progress unless all relevant agencies are committed

Why is it so hard for Federal agencies to share data with each other?

- Overlapping “turf” issues between agencies
- Stove-Pipes of Excellence within agencies
- Individual career concerns (publish or perish)
- The Diode Effect (one-way information transfers)

National Biosurveillance Integration System:
NBIS (but the “I” is silent…)

The Implementation Plan for the National Biosurveillance Strategy has to make some tough calls

- Break some historical turf boundaries
- End some pet projects
- Achieve actual timely data sharing (among Feds, and with States)
- Define some clear Big Science goals that are scientifically defensible and involve multiple agencies
- Provide some end-to-end authority
- Determine how to fund the necessary work